Digitized by Arya Samaj Foundation Chennai and eGangotri

Pharmacopoeia of India

(The Indian Pharmacopoeia)

PUBLISHED BY THE CONTROLLER OF PUBLICATIONS, DELHI

1985

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Pharmacopoeia of India

(The Indian Pharmacopoeia)

Digitized by Arya Samaj Foundation Chennai and eGangotri

CC-0. Prof. Satya Vrat Shastri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

R
615.19
IND-P.1:2

108834

R
615.19
IND-P.1:2
पुस्तकालय
गुरुकुल कांगड़ी विश्वविद्यालय
विषय संख्या
आगत नं० 108834
लेखक India, Ministry of Health.
शीर्षक Pharmacopoeia of India.

दिनांक	सदस्य संख्या	दिनांक	सदस्य संख्या

गुरुकुल कांगड़ी विश्वविद्यालय
कृपया पुस्तक के ऊपर कोई निशान आदि न लगायें।

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

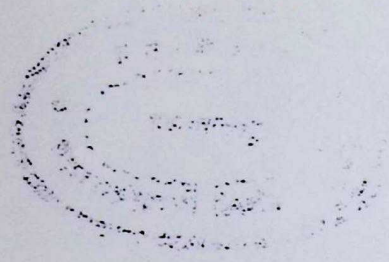
BOOKS FOR DISPLAY
1994-95

Stock Verification-2024

Stock Verification-2024

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri



CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Pharmacopoeia of India
(The Indian Pharmacopoeia)

Third Edition

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

615.19
IND P.1

Digitized by Arya Samaj Foundation Chennai and eGangotri

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

R615.19, IND-P.1:2
108834
Reserved for Departmental Library.....

PDGHS. 73
10,000 – 1984 (DSK II)

© Government of India

Ministry of Health & Family Welfare

108834

Pharmacopoeia of India

(The Indian Pharmacopoeia)

Volume – I
(A – P)

108834

Third Edition

PUBLISHED BY THE CONTROLLER OF PUBLICATIONS, DELHI

1985

JAIN BOOK AGENCY
C-9, Connaught Place, New Delhi-1
Ph.: 3320806, 3321663, 3326728
Gram : GOVTBOOK

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Price for Vol. I & Vol. II : *Inland* – Rs. 225.00

Foreign – £ 15.00

$ 18.00

R
615.19
IND-P.1:2

Designed & Produced by : PUBLICATIONS & INFORMATION DIRECTORATE (CSIR)

Designed & Produced by : GOVERNMENT OF INDIA
MINISTRY OF HEALTH & FAMILY WELFARE

PRINTED BY THE MANAGER, GOVT. OF INDIA PHOTOLITHO PRESS, FARIDABAD

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

LEGAL NOTICES

In India there are laws dealing with certain of the substances which are the subject of monographs which follow. These monographs should be read subject to the restrictions imposed by those laws wherever they are applicable.

It is expedient that enquiry be made in each case in order to ensure that the provisions of the law are being complied with.

In general, the Drugs & Cosmetics Act 1940, the Dangerous Drugs Act 1930 and, the Poisons Act 1919 and the rules framed thereunder should be consulted.

Under the Drugs & Cosmetics Act, the Indian Pharmacopoeia is the book of standards for drugs included therein and the standards as included in the Indian Pharmacopoeia would be official. If considered necessary these standards can be amended and the Secretary of the Indian Pharmacopoeia Committee is authorised to issue such amendments. Whenever such amendments are issued, the Indian Pharmacopoeia would be deemed to have been amended accordingly.

PATENTS AND TRADEMARKS

The inclusion in the Indian Pharmacopoeia of any drug subject to actual, or potential, patent or similar rights, or the inclusion of any name which is a trademark in any part of the world does not and shall not be deemed to imply or convey permission, authority, or licence to exercise any right or privilege protected by such patent or trademark, including licence to manufacture, without due permission, authority, or licence from the person or persons in whom such rights and privileges are vested.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Preface

The Government of India constituted a permanent Indian Pharmacopoeia Committee in 1948 for preparing the Indian Pharmacopoeia and keeping it up-to-date. The first edition of the Indian Pharmacopoeia was published in 1955, followed by a Supplement in 1960. The second edition of the Indian Pharmacopoeia and its Supplement were published in 1966 and 1975 respectively.

The Government of India, Ministry of Health & Family Welfare, vide their Resolution No. X.19014/1/77–D & MS dated 30th June, 1978,reconstituted for a period of five years the Indian Pharmacopoeia Committee for preparation of the third edition of the Indian Pharmacopoeia. The composition of the Committee is as follows:

Chairman	Dr Nitya Nand, Ph.D., F.N.A. Director Central Drug Research Institute Lucknow
Member	Dr K V Thiruvengadam, B.Sc., M.D., F.A.M.S Professor of Medicine Madras Medical College, and Physician, Government General Hospital Madras
Member	Dr M M S Ahuja, F.R.C.P. (Lond.), F.A.M.S. Professor and Head of the Department of Medicine All-India Institute of Medical Sciences New Delhi
Member	Dr P C Dandiya, Ph.D. (Toronto), F.A.M.S. Professor of Pharmacology S.M.S. Medical College Jaipur
Member	The Commissioner Food & Drugs Administration (Maharashtra State) Bombay
	Shri V C Sane, B.Sc., B.Sc. (Tech.), LL.B., Dip. B.M. (From 30th June, 1978 to 31st October, 1981)
	Shri S D Bhirud, B.Sc. (Hons.), M.Sc. (Tech.) (From 1st November, 1981)
Member	The Director Central Drugs Laboratory Calcutta Dr S K Roy, M.Sc., Ph.D., F.I.C.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Member	Director Central Indian Pharmacopoeia Laboratory Ghaziabad Dr P R Pabrai, M. Pharm., Ph.D.
Member	Director Central Research Institute Kasauli Dr M Balasubrahmanyan, M.B.B.S., M.D. (From 30th June, 1978 to 31st March, 1980) Dr S N Saxena, M.B.B.S., M.D., Dip. Bact. (From 1st April, 1980)
Member	Dr M A Patel, M. Pharm., Ph.D. Director Food & Drugs Control Administration (Gujarat State) Ahmedabad
Member	Dr J M Katyal, M.Sc. (Tech.), Ph.D. Managing Director Orissa Drugs & Chemicals Limited Bhubaneswar
Member	Shri R S Iyer, M.Sc., M. Chem. A., F.R.S.C. Director Corporate Quality Assurance Glaxo Laboratories (India) Limited Bombay
Member	Dr D S Bhate, B.Sc., B.Sc. (Tech.), Ph.D. (Bom)., Ph.D. (Lond.) Director Research & Development Unique Chemicals Bombay
Member	The Chief Inspector Chief Inspectorate of Materials (Ministry of Defence) Kanpur Dr D K Murty, M.Sc., D. Phil.
Member	Dr K P Bhargava, M.D., Ph.D. (Utah), F.A.M.S., F.N.A. Professor of Pharmacology and Principal K G Medical College Lucknow
Member Secretary	Dr S S Gothoskar, M.Sc. (Tech.), Ph.D. (Wisconsin) The Drugs Controller (India) Directorate General of Health Services New Delhi
Assistant Secretary	Shri Arun K. Shrivastava, M.Pharm.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

The Committee appointed the following Sub-committees

1. *Clinical Medicine and Pharmacology Sub-committee*

   Dr M M S Ahuja (Chairman), Dr K V Thiruvengadam.
   Dr K P Bhargava, Dr R R Chowdhury, Dr K G Nair

2. *Biological Products and Bio-assay Sub-committee*

   Dr M Balasubrahmanyan (*Chairman*), Shri Y S Nimbkar.
   Dr V R Kalyanaraman, Dr H M Bhatia, Dr B N Dhawan.
   Dr A D Nadkarni

3. *Antibiotics Sub-committee*

   Dr V C Vora (*Chairman*), Dr M K Majumdar, Dr (Smt) Gian Wati.
   Shri B N Thakore, Dr D Chakravarty, Dr I P Buch.
   Shri Santosh Yellore

4. *Synthetic Drugs Sub-committee*

   Dr S K Roy (*Chairman*), Dr G Ramana Rao, Dr S C Sharma.
   Dr S K Ramanathan, Dr Yusuf Hamied

5. *Medicinal Plants, Galenicals and Surgical Dressings Sub-committee*

   Dr C K Atal (*Chairman*), Miss S Satkopan, Dr S P Popli.
   Shri G C Tandon, Dr S N Iyer, Shri S Sen, Dr A Patani.
   Shri G D Parekh

6. *Chemicals and Pharmaceutical Aids Sub-committee*

   Dr D S Bhate (*Chairman*), Dr R N Dhar, Dr J L Sipahimalani.
   Dr A C Mulgaonkar, Shri V G Kudalkar, Shri A Banerjee

7. *Parenteral and Sterile Products Sub-committee*

   Dr J M Katyal (*Chairman*), Dr M A Patel, Shri P N Luthra,
   Shri Praful D Sheth, Dr J M Patel

8. *Non-Parenteral Products Sub-committee*

   Shri Amrut Mody (*Chairman*), Dr K N Kaul, Dr Parvinder Singh.
   Shri N M Dave, Shri J C Bhat, Shri S K Borkar, Dr B D Miglani

9. *Analytical Methods, Reagents, Diagnostic Aids and Containers Sub-committee*

   Shri R S Iyer (*Chairman*), Dr P R Pabrai, Dr P C Bose,
   Shri M R Shastri, Shri B N Thakore, Shri V M Shah, Dr Ajit Dangi

10. *Nomenclature and Formulae Sub-committee*

    Dr Harkishan Singh (*Chairman*), Dr R S Kapil.
    Shri R Balasubramanyan

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

In order to expedite the preparation of the third edition of the Indian Pharmacopoeia, the Committee constituted a Working Group for preparing the draft monographs and appendices, to examine the comments received on these and to make suitable recommendations thereon to the Committee.

The Composition of the Working Group is as under:

Shri V C Sane (*Chairman*, up to 31st October, 1981), Shri R S Iyer, Dr D S Bhate, Dr J L Sipahimalani, Shri R C Mehta, Shri M R Shastri, Dr A D Nadkarni, Shri B N Thakore, Dr Ajit Dangi, Shri S D Bhirud (*Chairman*, from 16th April, 1982).

The Monographs, Appendices and General Notices, as prepared by the Working Group and finalised by the Committee, are published by the Government in the form of the Pharmacopoeia of India, Third Edition.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Acknowledgements

In the course of preparing this Pharmacopoeia, the British Pharmacopoeia, the European Pharmacopoeia, the United States Pharmacopoeia, the International Pharmacopoeia, the State Pharmacopoeia of the USSR, the Japanese Pharmacopoeia, the British Pharmaceutical Codex, the Pharmaceutical Codex, the National Formulary (USA), the Merck Index and the standards published by the Indian Standards Institution have been consulted. The Indian Pharmacopoeia Committee expresses its thanks to the Commissions or Committees or Conventions or other organisations under whose authority these publications have been issued. At the same time the Committee wishes to stress that if any errors have inadvertently crept into the present compilation with regard to the statement of quantities or strengths or making quotations, such mistakes are in no way attributable to any of the publications mentioned above or the authorities issuing them. The Committee also acknowledges its gratitude to the members of the Sub-committees, and many others in the pharmaceutical industry, drug control laboratories and research and teaching institutions who have actively co-operated in the preparation of this edition. The Committee would like to place on record its deep appreciation of the contribution made by the Working Group, particularly Shri R S Iyer and his Secretariat staff, specially Smt I Vaz, and the staff of the Indian Pharmacopoeia Committee for preparing the monographs, and Drs M C Bhatia and Z Imam for checking all the monographs.

The Indian Pharmacopoeia Committee records its profound gratitude to Shri Y R Chadha, Editor-in-Chief, Publications & Information Directorate, Council of Scientific & Industrial Research, New Delhi, for accepting this challenging job, involving voluminous work and tight schedule.

The completion of this publication could be possible only through the dedicated work put in by Shri S N Saxena, Production Officer, Shri Pradeep Kumar Sharma and Miss Supriya Sahu, from Publications & Information Directorate, CSIR. The Committee would like to express its appreciation for the care exercised by Shri Saxena in maintaining the quality of the job and vigilance exercised in style editing and making the manuscript press ready, selecting suitable typography and layout and checking the proofs through the press.

The Committee also acknowledges the excellent cooperation extended by Mr Mohan Makhijani, Rekha Printers Pvt Ltd, New Delhi, for maintaining the standard of fine printing.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Contents

VOLUME ONE

	Page
Legal Notices	(v)
Preface	(vii)
Acknowledgements	(xi)
Introduction	(xv)
General Notices	1
Monographs (A—P)	15

VOLUME TWO

Monographs (Q — Z)	433
APPENDICES	A-1
Contents of Appendices	A-3
INDEX	I-1

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Introduction

Since the publication of the second edition of Indian Pharmacopoeia in 1966, the pharmaceutical industry in India has made substantial progress and many drugs are being produced in the country from basic stages. While the standards laid down in the earlier editions of the Pharmacopoeia were based mainly on imported drugs, the standards laid down in the third edition of the Indian Pharmacopoeia are essentially pertaining to those manufactured in India. As the Indian Pharmacopoeia is the statutory book of standards under the Drugs & Cosmetics Act, 1940 and the pharmaceutical manufacturers have to conform to these standards, the pharmaceutical industry has been actively associated in the preparation of this edition. Methods of analysis have been included in this edition which are capable of being adopted by a large segment of the pharmaceutical industry. Classical procedures, which have been replaced by the modern sophisticated instrumental techniques in the Pharmacopoeias of developed countries, have been retained due to economical and technical constraints. At the same time, instrumental techniques, such as ultra-violet and infra-red spectroscopy, gas-liquid chromatography, fluorescence spectrophotometry, atomic absorption spectrophotometry, etc. have been widely adopted in the current edition.

Format

The format of the monographs has been changed; wherein the portion forming a part of the mandatory specifications has been given in one place under the heading 'Standards'. The informative portion comprises synonym, if any, molecular weight, molecular formula and structure, description including nomenclature, solubility, category, dose and storage conditions. Description usually forms a part of the informative portion in the monographs but in certain specific cases like Liquorice and Carbenicillin Injection, etc., where it has beenconsidered important, description has been mentioned under 'Standards'. As far as possible, nomenclature of organic chemical drugs has been based on the IUPAC system.

Changes

Some changes have been made in this edition. The analytical techniques of flame photometry, fluorometry, electrophoresis and photometric haemoglobinometry have been accorded official recognition for the first time. The test for uniformity of content has been introduced for tablets where the content of active ingredient(s) in the tablets is 10 mg and less. Thus this test is included for:

Acetomenaphthone Tablets
Amitriptyline Tablets
Atropine Sulphate Tablets
Betamethasone Sodium Phosphate Tablets
Betamethasone Tablets
Bethanidine Tablets
Bisacodyl Tablets
Chlordiazepoxide Tablets
Chlorpheniramine Tablets

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Chlorpromazine Tablets
Clonidine Tablets
Cortisone Tablets
Cyproheptadine Tablets
Dehydroemetine Tablets
Dexamethasone Tablets
Diazepam Tablets
Dienoestrol Tablets
Digitoxin Tablets
Digoxin Tablets
Ergometrine Tablets
Ergotamine Tablets
Ethinyloestradiol Tablets
Ethyloestranol Tablets
Fludrocortisone Tablets
Fluphenazine Tablets
Folic Acid Tablets
Glibenclamide Tablets
Glyceryl Trinitrate Tablets
Guanethidine Tablets
Imipramine Tablets
Isocarboxazid Tablets
Isoprenaline Tablets
Isosorbide Dinitrate Tablets
Lanatoside C Tablets
Methadone Tablets
Methanedienone Tablets
Methotrexate Tablets
Methylergometrine Tablets
Nicoumalone Tablets
Norethisterone Tablets
Oxyphenonium Bromide Tablets
Prednisolone Tablets
Prednisone Tablets
Primaquine Tablets
Promethazine Tablets
Propranolol Tablets
Pyridoxine Tablets
Reserpine Tablets
Riboflavine Tablets
Salbutamol Tablets
Scopolamine Hydrobromide Tablets
Stilboestrol Tablets
Thiamine Hydrochloride Tablets
Thyroxine Tablets

As conventional chemical tests are not sufficiently specific to distinguish different sulphonamides, the infra-red spectroscopic test has been specified in the monographs of Sulphadimethoxine, Sulphadoxine, Sulphalene and Sulphamethizole.

A beginning has been made by the introduction of the dissolution test in respect of the tablets of Chlorpropamide, Digitoxin, Digoxin, Lithium Carbonate, Quinidine, Tetracycline and Tolbutamide.

A new appendix on pharmaceutical containers has been added; a test for estimation of arsenic which may be leached out into the injectable preparations from the glass containers has also been introduced in this appendix. Closures for injections should conform to certain special requirements like self-sealability and non-fragmentation. In addition, the water-extractable matter from the closures should comply with the tests for appearance, reducing substances, light transmission, heavy metals, pH, total ash and biological safety. These tests have been described in a separate appendix

A microbial limit test has been prescribed for certain pharmaceutical aids and oral liquid preparations, e.g. Acacia Powder, Aluminium Hydroxide Gel, Dried Aluminium Hydroxide Gel, Gelatin, Guar Gum, Milk of Magnesia, Starch, Powdered Tragacanth and Dried Yeast.

Methods of sterilization, which were previously a part of the monograph on Injections, have been described in a new appendix. New

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

appendices have alsobeen included in respectof determinationof thiomersal, phenol, aluminium and test for colony-forming units in vaccines and sera, wherever applicable. Biological assay of human antihaemophilic fraction and test for haemolysins form the subject of two new appendices. Consequent upon the introduction of long-acting insulin preparations in the Pharmacopoeia, tests for determining prolongation of insulin effect and for insulin in solution have also been prescribed in the appendices. Details of the methods for the determination of amylase activity and proteolytic activity and for the identification of steroids have been spelled out in detail in separate appendices.

The specifications for apparatus commonly used have been given in appendices on Nessler cylinders, thermometers, ultra-violet lamps, volumetric glassware, weights and balances. One of the essentials for good analysis is clean glassware; it has therefore been thought advisable to introduce an appendix on 'Cleaning of glassware' which describes the common methods for cleaning glassware used in chemical and microbiological operations.

Water is required for a variety of purposes ranging from manufacturing processes to the preparation of the final dosage forms. The quality of water therefore assumes considerable importance. The new appendix on 'Water for pharmaceutical use' clarifies the official standards in respect of 'Purified Water', 'Water for Injection' and 'Sterile Water for Injection'.

The monograph on Crystal Violet has undergone a major revision by the introduction of the thin-layer chromatographic test for detection and identification of related substances and by replacement of the existing chemical method of assay by a microbiological one with a view to differentiating Crystal Violet from methyl violet. The monograph on Starch has been revised so that description of the different varieties of starch, viz. maize, rice, wheat and potato has been added as a part of the Standards. The two separate monographs on Indian Gum and Indian Gum Powder have been combined together in the monograph on Acacia.

The two separate monographs on Rabies Vaccine – BPL-inactivated Rabies Vaccine and Carbolised Rabies Vaccine have been combined into one entitled 'Rabies Vaccine'. On the other hand, the single monograph on Calciferol in the second edition has been replaced by two monographs, 'Cholecalciferol' and 'Ergocalciferol'.

The appendix entitled 'Statistical methods in biological assays', described in the second edition of the Indian Pharmacopoeia, has been replaced by an extensively revised appendix entitled 'Design and analysis of biological assays'. Similarly, the combined appendix on 'Powders and Sieves' given in the earlier editions of I.P. has been split into two appendices entitled 'Sieves' and 'Powder fineness', the fineness of powder being assessed on the basis of the average nominal aperture of the sieves.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Gas-liquid chromatography has been recognised as an alternative method for determination of alcohol. The Pyrogen test has been revised to make the test less time-consuming than the previous method.

The disintegration test has been amended by modifying the design of the apparatus and method of testing. Similarly, the test for absorbancy for Absorbent Cotton Wool has been revised. The test for determination of viscosity has also been modified by the introduction of other methods for determination of viscosity in addition to the existing method involving the use of Ostwald viscometer.

Wherever possible, chemical and spectrophotometric methods have been given as alternative to microbiological methods of assay in respect of antibiotics. It has, however, to be pointed out that in case of any dispute the results of microbiological assay will prevail.

The practice of not permitting addition of colours to or coating of tablets unless specified in the individual monograph, has been continued in this edition also.

The names of the following drugs have been changed in this Edition

Names as given in I.P. Second Edition	*Names as given in I.P. Third Edition*
Acetylsalicylic Acid	Aspirin
Acetylsalicylic Acid Tablets	Aspirin Tablets
Acetylsalicylic Acid Tablets, Soluble	Soluble Aspirin Tablets
Calcium Chloride Hydrated	Calcium Chloride
Formolised Plague Vaccine	Plague Vaccine
Human Normal Serum Albumin Injection	Human Normal Serum Albumin
Human Normal Immuno-globulin Injection	Human Normal Immuno-globulin
Hyoscine Hydrobromide	Scopolamine Hydrobromide
Indian Gum	Acacia
Normal Human Plasma	Human Plasma
Purified Talc	Talc
Sodium Citrate Anticoagulant Injection	Anticoagulant Sodium Citrate Injection
Thyroxine Sodium Tablets	Thyroxine Tablets
d-Tubocurarine Chloride	Tubocurarine Chloride

A list of items included in the Second Edition of the Indian Pharmacopoeia, but not included in this edition is given below:

Omissions

Acetic Acid	*Acetylsalicylic Acid Tablets, Compound
Acetic Acid, Dilute	Aconite
Acetic Acid, Glacial	

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Aconite Liniment
Aconite Tincture
Activated Wood Charcoal
Adrenaline Malate Injection
Agar
Agar Powder
Ajowan Oil
Alcohol, Dilute
Aloes
Aloes Powder
Aloin
Alum
Amethocaine Hydrochloride
Amethocaine Injection
Amidopyrine
Aminacrine Hydrochloride
Ammonia Solution, Strong
Ammonia Solution, Dilute
Ammoniated Mercury
Ammoniated Mercury Ointment
Ammonium Acetate Solution, Strong
Ammonium Bicarbonate
Ammonium Chloride Tablets
Aromatic Spirit of Ammonia
Amphetamine Sulphate
Amphetamine Sulphate Tablets
Amyl Nitrite
Anise Oil
Antazoline Hydrochloride
Antazoline Tablets
Antimony Sodium Tartrate
Antimony Sodium Tartrate Injection
Antitoxins
Apomorphine Hydrochloride
Apomorphine Injection
Ashoka
Ashoka Liquid Extract
Aswagandha
Aswagandha Liquid Extract
Atropine

Bacitracin Tablets
Bacterial Vaccines
Bael
Bael Liquid Extract
Barbitone Sodium
Barbitone Sodium Tablets
Barium Sulphate Compound Powder
Belladonna Herb Powder
Belladonna Tincture
Belladonna Herb, Prepared
Belladonna Root
Belladonna Root Powder
Belladonna Liniment
Belladonna Liquid Extract
Bemegride
Bemegride Injection
Benzoin
Benzoin Tincture, Compound
Bismuth Sodium Tartrate
Bismuth Sodium Tartrate Injection
Bismuth Subcarbonate
Bismuth Subgallate
Black Catechu
Borax
Borax Glycerin
Brilliant Green
Burnt Sugar
Butacaine Sulphate

Caffeine Citrate
Calamine Lotion
Calcium Mandelate
Calcium Phosphate
Camphor
Camphor Liniment, Ammoniated
Camphor Liniment
Camphor Water
Camphorated Opium Tincture
Cannabis
Cannabis Extract
Capsicum
Capsicum Powder
Capsicum Oleoresin
Capsicum Tincture
Caraway
Caraway Powder
Caraway Oil
Carbachol
Carbachol Injection
Carbachol Tablets
Carbon Dioxide
Cardamom Fruit
Cardamom Tincture, Compound
Cassia Cinnamon
Cassia Cinnamon Powder
Cassia Fruit
Cassia Pulp
Cassia Oil
Chaulmoogra Oil

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Chenopodium Oil
Chiniofon Sodium
Chirata
Chirata Infusion, Compound
Chirata Infusion, Concentrated Compound
Chlorinated Lime
Chloroform Water
Chlorophenothane Application
Chlortetracycline Capsules
Chlortetracycline Hydrochloride
Chlortetracycline Injection
Cholera Vaccine Formolised
Chrysarobin
Chrysarobin Ointment
Cinchocaine Hydrochloride
Cinchona
Cinchona Extract
Cinchona Powder
Cinchona Tincture, Compound
Cinchona Febrifuge
Cinnamon
Cinnamon Leaf Oil
Cinnamon Oil
Cinnamon Powder
Clove
Clove Powder
Coal Tar, Prepared
Coal Tar Solution
Cocaine
Cocaine Eye Ointment
Cocaine Hydrochloride
Codein Tablet Compound
Copper Sulphate
Coriander
Coriander Powder
Coriander Oil
Creosote
Cyclobarbitone

Datura Herb
Datura Liquid Extract
Datura Tincture
Dexamphetamine Sulphate
Dexamphetamine Sulphate Tablets
Digitalis
Digitalis Powder
Digitalis Prepared
Digitalis Tablets
Digitalis Tincture
Digitoxin Injection
Dihydrostreptomycin Sulphate
Dihydrostreptomycin Sulphate Injection
Dill
Dill Powder
Dill Oil
Dill Water Concentrated
Dioctyl Sodium Sulphosuccinate
Diphtheria Vaccine Plain
Diphtheria Vaccine Adsorbed
Diphtheria Tetanus & Whooping Cough Vaccine
Dithranol Ointment

Elixir Simple
Emulsifying Ointment
Emulsifying Ointment, Hydrous
Ephedra
Ergot
Ergot, Prepared
Ergot Tablets
Ethanolamine
Ethanolamine Oleate Injection
Ether, Spirit of
Ether, Solvent
Ethisterone
Ethisterone Tablets
Evans Blue
Extracts

Fennel
Fennel Oil
Fennel Powder
Flexible Collodion
Formaldehyde Solution

Gelatin, Zinc
Gelatin Sponge, Absorbable
Ginger
Ginger Powder
Ginger Syrup
Ginger Tincture, Strong
Glycerin Suppositories
Glycobiarsol
Glycobiarsol Tablets

Hexachlorophene
Hexamine
Hexoestrol
Hexoestrol Tablets
Honey
Human Serum, Dried

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Human Serum, Liquid
Hyoscyamus
Hyoscyamus Liquid Extract
Hyoscyamus Powder
Hyoscyamus Tincture
Hypophosphorous Acid

Ichthammol
Indian Gum Mucilage
Indigo Carmine
Iodine Solution, Aqueous
Iodine Solution, Strong
Iodine Solution, Weak
Iodised Oil Injection
Iodophthalein
Iodoxyl
Iodoxyl Injection
Ipecacuanha and Opium Powder
Ipecacuanha and Opium Tablets
Ipecacuanha Liquid Extract
Ipecacuanha Powder
Ipecacuanha, Prepared
Ipecacuanha Tincture
Iron and Quinine Citrate
Isapgol

Jatamansi

Kalmegh
Kalmegh Liquid Extract
Kaolin Poultice
Kokum Butter
Kurchi
Kurchi Bismuth Iodide
Kurchi Liquid Extract

Lead Acetate
Lead Subacetate Solution, Strong
Lead Subacetate Solution, Dilute
Lead Monoxide
Lemon Grass Oil
Lemon Oil
Lemon Peel, Fresh
Lignocaine Injection
Linseed
Linseed, Crushed
Linseed Oil
Liquorice Powder
Liquorice Compound Powder
Liquorice Liquid Extract
Liver Injection Crude
Liver, Proteolysed
Lobelia
Lobeline Hydrochloride
Lobeline Injection
Lotions

Magnesium Sulphate, Dried
Male Fern
Male Fern Powder
Male Fern Extract
Malic Acid
Menadione Sodium Bisulphite
Menadione Sodium Bisulphite Injection
Mepacrine Hydrochloride
Mepacrine Tablets
Mercaptomerin Sodium
Mercuric Oxide, Yellow
Mercuric Oxide Eye Ointment
Mercurophylline
Mercurous Chloride
Mercury
Mercury, Oleated
Mercury with Chalk
Mersalyl Acid
Mersalyl and Theophylline Injection
Methoin
Methoin Tablets
Methylene Blue
Methyltestosterone
Methyltestosterone Tablets
Mild Silver Protein
Morphine Hydrochloride Solution
Mustard Oil, Expressed
Myrobalan
Myrobalan Powder, Compound
Myrobalan Small
Myrobalan Small Ointment
Myrobalan Small and Opium Ointment

Neem Oil
Nicotinamide Injection
Nutmeg
Nutmeg Oil
Nutmeg Powder
Nux Vomica
Nux Vomica Liquid Extract
Nux Vomica Powder
Nux Vomica Tincture
Nux Vomica, Prepared

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Octyl Nitrite
Ointment, Hydrous
Ointment, Simple
Opium Tincture
Opium Tincture, Camphorated
Orange Peel, Dried
Orange Peel, Fresh
Orange Tincture
Ouabain
Ouabain Injection

Papaverine
Papaverine Hydrochloride
Papaverine Injection
Paraffin (Liquid) Emulsion
Paraffin Ointment
*Penicillin Eye Ointment
*Phenacetin
Phenol Liquefied
Phenol Glycerin
Phenolsulphonphthalein
Phenylmercuric Nitrate
Phosphoric Acid, Dilute
Phthalylsulphacetamide
Picrorhiza
Picrorhiza Tincture, Compound
Piperazine Citrate Elixir
Podophyllum Resin
Posterior Pituitary Injection
Potassium Acetate
Potassium Acid Tartrate
Potassium Bicarbonate
Potassium Hydroxide
Potassium Hydroxide Solution
Procaine Benzylpenicillin Injection
Proflavine Hemisulphate
Progesterone
Progesterone Injection
Protein Hydrolysate Injection
Psoralea Fruits
Punarnava
Punarnava Liquid Extract
Pyrethrum
Pyrethrum Solution
Pyroxylin

Quillaia
Quillaia Powder
Quinine and Urethane Injection
Quinine Ethyl Carbonate
Quinine Hydrochloride
Quinine Hydrochloride Tablets

Rasna
Rauvolfia
Rauvolfia Dry Extract
Rauvolfia Liquid Extract
Rauvolfia Powder
Rauvolfia Tablets
Resorcinol
Rhubarb
Rhubarb Compound Powder
Rhubarb Powder
Riboflavine Injection

Salicylic Acid Ointment
Santonin
Saussurea
Saussurea Powder
Senna Leaf Powder
Sesame Oil
Shark Liver Oil with Malt Extract
Silver Protein, Mild
Silver Protein, Strong
Simple Ointment
Soap, Hard
Soap Liniment
Soap, Soft
Soda Lime
Sodium Bicarbonate Injection
Sodium Bicarbonate Tablets Compound
Sodium Bromide
Sodium Carbonate
Sodium Chloride Tablets
Sodium Citrate Tablets
Sodium Iodide
Sodium Nitrite
Sodium Perborate
Sodium Phosphate, Dried
Sodium Potassium Tartrate
Sodium Sulphate
Sodium Sulphate, Dried
Spirit, Specially Denatured
Staphylococcus Toxoid
Staphylococcus Vaccine
Stibophen
Stibophen Injection
Storax, Prepared
Stramonium
Stramonium Powder
Stramonium Liquid Extract
Stramonium Tincture

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Strychnine Hydrochloride
Strychnine Hydrochloride Solution
Sulphacetamide
Sulphaguanidine
Sulphaguanidine Tablets
Sulphur Ointment
Sulphur, Precipitated
Sulphur, Sublimed
Sulphuric Acid
Sulphuric Acid Aromatic
Sulphuric Acid, Dilute
Suppositories
Syrup

Tannic Acid
Tannic Acid Glycerin
Tar
Terpin Hydrate
Terpin Hydrate Elixir
Tetanus Toxoid
*Tetracycline Oral Suspension
Theobromine and Sodium Salicylate
Theophylline and Sodium Acetate
Tinctures
Tolazoline Hydrochloride
Tolazoline Tablets
Tolu Balsam
Tolu Syrup
Triethanolamine
Tryparsamide
Tryparsamide Injection

Turmeric
Turpentine Liniment
Turpentine Oil
Typhoid-Paratyphoid A & B Vaccine
Typhoid-Paratyphoid A, B & C Vaccine

Urea Stibamine
Urea Stibamine Injection
Urethane
Urginea
Urginea Tincture
Urginea Syrup
Urginea Vinegar

Vaccine Lymph
Valerian
Valerian Tincture Ammoniated
Vasaka
Vasaka Liquid Extract
Vasaka Syrup
Vidang
Vinyl Ether

Waters, Aromatic
Wood Charcoal, Activated
Wool Alcohols
Wool Alcohols Ointment
Whooping Cough Vaccine

Zinc Oxide Compound Paste
Zinc Oxide Ointment Hydrous
Zinc Oxide Ointment

These items have subsequently been deleted from the second edition of the Indian Pharmacopoeia.

A list of items not included in the Second Edition but added in this edition is given below:

Additions

Aluminium Sulphate
Amantadine Hydrochloride
Amantadine Hydrochloride Capsules
Amantadine Hydrochloride Syrup
Aminocaproic Acid
Aminocaproic Acid Injection
Aminocaproic Acid Tablets
Amoxycillin Trihydrate
Amoxycillin Capsules
Amphotericin B
Ampicillin for Oral Suspension
Amylase, Alpha
Anticoagulant Citrate Dextrose Solution
Anticoagulant Citrate Phosphate Dextrose Solution
Atropine Methonitrate

Bacitracin Zinc
Barium Sulphate for Suspension
Bendrofluazide

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Benzalkonium Chloride Solution
Benzathine Penicillin Injection
Benzathine Penicillin Injection, Fortified
Benzoic Acid Ointment, Compound
Berberine Chloride
Betamethasone Valerate
Bethanidine Sulphate
Bethanidine Tablets
Bisacodyl
Bisacodyl Tablets
Butylated Hydroxyanisole
Butylated Hydroxytoluene

Calcium Levulinate
Calcium Levulinate Injection
Calcium Pantothenate
Carbenicillin Disodium
Carbenicillin Injection
Carbimazole
Cellulose, Microcrystalline
Cellulose Acetate Phthalate
Cephalexin
Cephalexin Capsules
Cephalexin Tablets
Chloramphenicol Eye Ointment
Chloramphenicol Sodium Succinate
Choramphenicol Sodium Succinate Injection
Chloroquine Phosphate Injection
Chlorphenesin
Cholecalciferol
Cimetidine
Cimetidine Tablets
Citric Acid, Anhydrous
Clofazimine
Clofazimine Capsules
Clonidine Hydrochloride
Clonidine Tablets
Cyclobarbitone Calcium
Cycloserine
Cyproheptadine Hydrochloride
Cyproheptadine Hydrochloride Syrup
Cyproheptadine Tablets

Dehydroemetine Hydrochloride
Dehydroemetine Injection
Dehydroemetine Tablets
Dequalinium Chloride
Deslanoside
Deslanoside Injection
Diazepam Injection
Diethyltoluamide
Dimethicone, Activated
Diphenoxylate Hydrochloride
Diphenylpyraline Hydrochloride
Diphtheria and Tetanus Vaccine (Adsorbed)
Diphtheria, Tetanus and Pertussis Vaccine (Adsorbed)
Doxycycline Hydrochloride
Doxycycline Capsules

Ethacrynic Acid
Ethacrynic Acid Tablets
Ethionamide
Ethionamide Tablets
Ethopropazine Hydrochloride
Ethopropazine Tablets
Ethosuximide
Edetate Disodium
Ethyloestrenol
Ethyloestrenol Tablets

Fenfluramine Hydrochloride
Fenfluramine Tablets
Fludrocortisone Acetate
Fludrocortisone Tablets
Fluorouracil
Fluorouracil Injection
Fluphenazine Hydrochloride
Fluphenazine Hydrochloride Injection
Fluphenazine Tablets
Frusemide Injection
Furazolidone

Glibenclamide
Glibenclamide Tablets
Glyceryl Monostearate
Griseofulvin
Griseofulvin Tablets

Human Antihaemophilic Fraction, Dried
Human Plasma Protein Fraction
Hydralazine Hydrochloride
Hydroxyethyltheophylline

Ibuprofen
Ibuprofen Tablets

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Idoxuridine
Indomethacin
Indomethacin Capsules
Intraperitoneal Dialysis Fluid
Isophane Insulin Injection
Isocarboxazid
Isocarboxazid Tablets
Isoprenaline Hydrochloride
Isoprenaline Hydrochloride Injection
Isosorbide Dinitrate, Diluted
Isosorbide Dinitrate Tablets
Isoxsuprine Hydrochloride

Kanamycin Sulphate
Kanamycin Acid Sulphate
Kanamycin Injection

Lanatoside C
Lanatoside C Tablets
Levodopa
Levodopa Capsules
Levodopa Tablets
Lincomycin Capsules
Lincomycin Hydrochloride
Lithium Carbonate
Lithium Carbonate Tablets
Lynestrenol

Magnesium Chloride
Magnesium Stearate
Mannitol
Measles Vaccine, Live
Mebendazole
Mebendazole Tablets
Megestrol Acetate
Mercaptopurine
Mestranol
Metformin Hydrochloride
Methandienone
Methandienone Tablets
Methdilazine Hydrochloride
Methotrexate
Methotrexate Tablets
Methylergometrine Injection
Methylergometrine Maleate
Methylergometrine Tablets
Metronidazole Benzoate

Nalidixic Acid
Nalidixic Acid Tablets
Nandrolone Decanoate
Nandrolone Decanoate Injection
Nandrolone Phenylpropionate
Niclosamide
Niclosamide Tablets
Nitrofurantoin
Nitrofurantoin Tablets
Nitrofurazone
Norethisterone
Norethisterone Tablets
Noscapine
Nystatin
Nystatin Ointment
Nystatin Tablets
Nystatin Vaginal Tablets

Oxprenolol Hydrochloride
Oxprenolol Tablets
Oxytetracycline Eye Ointment

D-Panthenol
Penicillin Benzathine Injection
Penicillin Benzathine Fortified Injection
Pentamidine Isothionate
Pentazocine Hydrochloride
Phenformin Hydrochloride
Phenformin Tablets
Phentolamine Hydrochloride
Phentolamine Mesylate
Phenylbutazone
Phenylbutazone Tablets
Phenylephrine Hydrochloride
Phenylephrine Injection
Phenylmercuric Acetate
Phenytoin Injection
Pholcodine
Piperazine Hydrate
Poliomyelitis Vaccine (Oral)
Polyethylene Glycol 1500
Polyethylene Glycol 4000
Polyethylene Glycol 6000
Polysorbate 20
Polysorbate 80
Polyvinylpyrrolidone
Pralidoxime Chloride
Pralidoxime Chloride Injection
Primaquine Phosphate
Primaquine Tablets
Prochlorperazine Injection
Prochlorperazine Maleate
Prochlorperazine Mesylate

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Prochlorperazine Tablets
Promethazine Theoclate
Propantheline Bromide
Dextropropoxyphene Hydrochloride
Dextropropoxyphene Napsylate
Propyl Gallate
Propylene Glycol
Pyrazinamide
Pyrazinamide Tablets
Pyrimethamine

Rabies Antiserum
Riboflavine Phosphate Sodium
Rifampicin
Rifampicin Capsules

Saccharin
Salbutamol Sulphate
Salbutamol Tablets
Scopolamine
Shellac
Snake Venom Antiserum
Sodium Acetate
Sodium Ascorbate
Sodium Carboxymethylcellulose
Sodium Cromoglycate
Sodium Cromoglycate Cartridges
Sodium Lactate Injection
Sorbitol
Sorbitol Solution
Spironolactone
Stilboestrol Diphosphate
Succinylcholine Chloride
Succinylcholine Chloride Injection
Sulphadoxine
Sulphalene
Sulphamethizole
Syrups

Tartaric Acid
Tetanus Vaccine, Adsorbed
Tetramisole Hydrochloride
Thiabendazole
Thiabendazole Tablets
Thiomersal
Titanium Dioxide
Tocopheryl Acetate
Tragacanth
Triamcinolone
Triamcinolone Acetonide
Triamcinolone Tablets
Triamterene
Triamterene Capsules
Trifluoperazine Hydrochloride
Triflupromazine Hydrochloride
Typhoid Vaccine

Vanillin
Verapamil Hydrochloride
Verapamil Injection
Verapamil Tablets

Water for Injection, Sterile

Yeast, Dried

Zinc Chloride

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Pharmacopoeia of India
(The Indian Pharmacopoeia)

Volume –I
(A–P)

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

General Notices

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

The General Notices provide the basic guidelines for the interpretation and application of the standards, tests, assays and other specifications of the Pharmacopoeia of India.

Title

The full title of this book, including supplements thereto, is the Pharmacopoeia of India, Third Edition. This title may be abbreviated to Indian Pharmacopoeia, Third Edition. When the term I.P. is used, without further qualification during the period in which this pharmacopoeia is official, it refers to the Pharmacopoeia of India, Third Edition.

Capital Letters in the Text

The names of the Pharmacopoeial drugs, preparations, substances and processes occurring in the text of the Pharmacopoeia are printed with capital initial letters and these infer that materials of pharmacopoeial quality must be used. For example, in the statement "Adrenaline Tartrate Injection is a sterile solution of Adrenaline Bitartrate with Sodium Metabisulphite and Sodium Chloride in Water for Injection" the capital initial letters of the substances indicate that Adrenaline Bitartrate, Sodium Metabisulphite, Sodium Chloride and Water for Injection to be used are those of the Pharmacopoeia.

Italics

Italic types have been used for the systematic names of plants and micro-organisms, and for some sub-headings and some parts of the chemical names.

Italic types have also been used for words which refer to reagents, substances or processes, described or defined in an Appendix. For example, in the statement *mercuric sulphate solution* the solution of mercuric sulphate to be used is that of the Appendix.

Official and Official Articles

The word 'official' wherever used in this Pharmacopoeia, or with reference thereto, is synonymous with 'Pharmacopoeial'. The designation I.P. in conjunction with the official title on the label of an article is a reminder that the article purports to comply with I.P. standards.

The following terms are used where the articles for which monographs are provided are to be distinguished:

A drug substance is a single drug or a drug entity for which the monograph title includes no indication of the nature of a dosage form.

A dosage form is the finished or partially finished preparation or product of one or more drug substances formulated for use on the patient.

An article is an item for which a monograph is provided, whether a drug substance or a dosage form.

Added Substances

An official drug substance, as distinguished from a dosage form, contains no added substances except where specifically permitted in the individual monograph. Where such addition is permitted, the label indicates the name(s) and amount(s) of any added substance(s).

Unless otherwise specified in the individual monograph, or elsewhere in the General Notices, suitable substances, such as bases, carriers, coatings, preservatives, stabilisers, vehicles and other pharmaceutical aids may be added to a Pharmacopoeial dosage form or finished

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

device to enhance its stability, usefulness or elegance, or to facilitate its preparation. Such substances shall be harmless in the amounts used, shall not exceed the minimum quantity required to provide their intended effect, shall not impair the therapeutic efficacy of the dosage form, and shall not interfere with the tests and assays prescribed for determining compliance with the official standards.

The addition of colouring and flavouring agents, unless permitted in the individual monograph, or general monographs, is not official. Where the addition of colouring is permitted, any colouring agent used shall be one that is included in the list of colours prescribed under the Drugs and Cosmetics Rules, 1945.

Vegetable Drugs

The macroscopical description of a vegetable drug includes those features which can be seen by the unaided eye or by the use of a hand lens. The diagnostic characteristics given under a powdered vegetable drug are to be read in conjunction with the microscopical description given under the whole drug.

Vegetable drugs are required to be free from insects and other animal matter, and from animal excreta. Not more than traces of foreign organic matter may be present in powdered vegetable drugs.

MONOGRAPHS

Titles of Monographs

The main titles of monographs in the Pharmacopoeia are given in English. Subsidiary titles or synonyms, where included, have the same significance as the main titles.

Chemical Formulae

When the chemical composition of an official substance is known or generally accepted, the graphic and molecular formulae and the molecular weight are given at the beginning of the monograph. This information refers to the chemically pure substances and is not to be regarded as an indication of the purity of the drug. From the statements of standards of purity and strength and in descriptions of processes of assay, it will be evident from the context that the formulae denote the chemically pure substances.

Chemical Names

Chemical names have been provided in the monographs which have titles which specify substances that are distinctly definable chemical entities. These are the names sanctioned and employed by the International Union of Pure and Applied Chemistry (IUPAC).

Atomic Weights

The atomic weights adopted are the values given in the Table of Relative Atomic Weights 1975 published by the International Union of Pure and Applied Chemistry. The values are based on the carbon-12 scale.

Category

The statement of category is provided for information and is indicative of the medical or pharmaceutical basis for recognition in the Pharmacopoeia. It generally represents an application of the best known pharmacological action of the article or of its active ingredient. The statement is not intended to limit in any way the choice or use of the article nor to indicate that it has no other activity or use.

Doses

Doses mentioned in the Pharmacopoeia are intended merely for general guidance and represent, unless otherwise stated, the average range of quantities which are generally regarded as suitable for adults when

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

208/DGHS/ND/90—5,000 F.3

administered by mouth. They are not to be regarded as binding upon the prescribers. The oral doses may in many cases be repeated three to four times in twenty-four hours. It must not be assumed, however, that they indicate the greatest amounts of drugs that may be given. The medical practitioner will exercise his own judgement and act on his own responsibility in respect of the amount of any therapeutic agent he may prescribe or administer or the frequency of its administration. When, however, an unusually large dose appears to have been prescribed, it shall be the duty of the pharmacist to satisfy himself that the prescriber's intention has been correctly interpreted. If it is usual to administer a drug by a method other than by mouth, the single dose suitable for that method of administration is mentioned.

In some instances the doses given daily have been indicated. In the case of some preparations notes have been given below the statement of the doses to show the approximate quantities of active ingredients contained in the maximal doses. These are included for the guidance of the prescriber and are not to be regarded as statements of standards.

Usual Strength

The statement on the usual strength(s) of a dosage form, given in the individual monograph, indicates the strength(s) normally marketed and which the pharmacist should dispense when the strength has not been specifically mentioned by the prescriber.

Description

The description pertaining to an article is relatively general in nature. It is provided to indicate properties of an article complying with the standards given in the monograph. The properties are not in themselves standards or tests for purity even though they may help in the preliminary evaluation of the integrity of an article. Where, however, description is included under the heading 'Standards', the drug shall comply with this requirement.

Odour and Taste

Where a substance is described as 'odourless' under Description, the following method of examination applies:

Examine a sample of not more than 25 g immediately after opening the package. If any odour is noticeable, transfer the sample rapidly to an open container and re-examine after fifteen minutes. If the odour is still discernible, the sample does not comply with the description 'odourless'.

The terms 'odourless' or 'practically odourless' are descriptive only and are not to be regarded as standards of purity for a particular lot of an article, except in those cases where a particular odour is specifically prohibited in the monograph under 'standards'.

Statements on taste are provided only in cases where this property is a guide to the acceptability of the material. Such statements are not part of the official standards.

Solubility

The statements on solubility given under the heading 'Solubility' are not standards or tests for purity, but are provided primarily as information. Where, however, a quantitative solubility test is given under standards, the drug shall comply with this requirement.

Statements of solubilities are indicated by a descriptive phrase and are intended to apply at ambient temperature.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

The following table indicates the meanings of such phrases:

Descriptive phrase	Approximate quantities of solvent by volume for 1 part of solute by weight
very soluble	less than 1 part
freely soluble	from 1 to 10 parts
soluble	from 10 to 30 parts
sparingly soluble	from 30 to 100 parts
slightly soluble	from 100 to 1000 parts
very slightly soluble	from 1000 to 10,000 parts
insoluble practically insoluble	more than 10,000 parts

Official Standards

The standards of purity and strength stated in the monograph of the Pharmacopoeia apply to articles which are intended for medicinal use but not necessarily to articles which may be sold under the same name for other purposes.

All statements in the monographs given under the heading 'Standards' constitute standards for the official substances, and a substance is not of Pharmacopoeial quality unless it complies with all the requirements stated under 'Standards'. Monographs may also include information on chemical formula, molecular weight, category, doses, description and statements under the heading 'Solubility'

The requirements given in the monographs are not framed to provide against all possible impurities. It is not to be presumed, for example, that an unusual impurity is tolerated which is not precluded by the prescribed tests should rational considerations require that it be absent. The tests have been framed to summarise the impurities to which attention is more particularly needed, to fix the limits of those which are tolerated to a given extent, and to indicate convenient methods of ensuring the absence of certain others for which no tolerance is approved.

Expression of Standards

Where the standard for a substance described in a monograph is expressed in terms of the chemical formula for that substance and an upper limit is not stated, the upper limit is not more than the equivalent of 100.5 per cent. Similarly, when the standard is expressed in terms of the chemical formula for the anhydrous substance, the upper limit is not more than the equivalent of 100.5 per cent.

When a standard is required to be calculated with reference to the dried substance, the drying conditions set out in the test for 'Loss on drying' in the monograph apply. When the standard is to be calculated with reference to the anhydrous substance, the content of water is determined by the method given in the monograph. When the standard is to be calculated with reference to the solvent-free substance, the content of solvent is determined by the method described in the monograph.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Limits and Tolerances

When limits of content are given in a monograph they are determined by the method prescribed therein.

Where limits are expressed numerically, the upper and lower limits of a range are inclusive so that the range consists of the two values themselves and all intermediate values, but no values outside the limits. The limits expressed in monograph definitions and tests, regardless of whether the values are expressed as percentages or as absolute numbers, are considered significant to the last digit shown.

The limits and tolerances stated in the definitions in the monographs for Pharmacopoeial articles allow for analytical error, for unavoidable variations in manufacture and compounding, and for deterioration to an extent considered insignificant under practical conditions. No further tolerances should be applied to the values obtained in a test or assay to determine whether the article being examined complies with the requirements of the monograph.

Abbreviated Statements in Monographs

Incomplete sentences are employed in parts of the monographs for directness and brevity (for example, Iodine Value.....or Arsenic—Not more than.....parts per million). Where the tests are so abbreviated, it is to be understood that the page number shown designates the relevant procedure to be followed, and that the values specified are the required limits.

General Monographs

These are monographs which describe dosage forms and include requirements of general application and requirements of tests which apply to all the monographs for the relevant dosage forms, unless otherwise indicated in the individual monograph.

Other Requirements

In the monographs on dosage forms under the sub-heading 'Other requirements' are included the requirements of tests detailed in the general monographs on dosage forms such as Capsules, Injections, Tablets, etc.

TESTS AND ASSAYS

Apparatus : A specification for a definite size or type of container or apparatus in a test or assay is given merely as a recommendation. Where volumetric flasks or other exact measuring or weighing devices are specified, this or other equipment of atleast equivalent accuracy may be employed.

In order to obtain solutions having concentrations that are adaptable to the working range of the instrument being used, solutions of proportionally higher or lower concentrations may be prepared, according to the solvents and proportions thereof that are specified in the procedure.

Water-bath : The term 'water-bath' means a bath of boiling water, unless water at some other temperature is indicated. An alternative form of heating may be employed providing that the required temperature is approximately maintained but not exceeded.

Desiccator : The term 'desiccator' means a tightly-closed container of suitable size and design that maintains an atmosphere of low moisture content by means of silica gel or phosphorus pentoxide or other suitable desiccant.

Vacuum Desiccator : The term 'vacuum desiccator' means a desiccator

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

that maintains the low-moisture atmosphere at a reduced pressure of not more than 20 Torr or the pressure indicated in the individual monograph.

Expression of Strengths

In defining standards, the expression 'per cent' is used, according to circumstances, with one of four different meanings. In order that the meaning to be attached to the expression in each instance may be clear, the following notations are used:

Per cent w/w (percentage weight in weight) expresses the number of grams of active substance in 100 grams of product.

Per cent w/v (percentage weight in volume) expresses the number of grams of active substance in 100 millilitres of product

Per cent v/v (percentage volume in volume) expresses the number of millilitres of active substance in 100 millilitres of product.

Per cent v/w (percentage volume in weight) expresses the number of millilitres of active substance in 100 grams of product.

The strengths of solutions of solids in liquids are expressed as percentage weight in volume, of liquids in liquids as percentage volume in volume, and of gases in liquids as percentage weight in weight, and mixtures of solids and semi-solids as percentage weight in weight.

When the strength of a solution is expressed as parts of dissolved substance in parts of the solution, it is to be understood to mean parts by weight (grams) of a solid in parts by volume (millilitres) of the final solution, or parts by volume (millilitres) of a liquid in parts by volume (millilitres) of the final solution, or parts by weight (grams) of a gas in parts by weight (grams) of the final solution.

Limits of Impurities

In certain tests, the concentration of impurity represented by the test is given in parts per million by weight (ppm) or as a percentage. These figures are approximations only; acceptance or rejection is determined on the basis of compliance or otherwise with the stated test.

Percentage of Alcohol

All statements of percentages of alcohol, such as under the sub-heading 'Alcohol Content', refer to percentage, by volume, of C_2H_5OH at 15.56°. Where reference is made to 'C_2H_5OH', the chemical entity possessing absolute (100 per cent) strength is intended.

Reagents and Solutions

The proper conduct of the tests and assays of the Pharmacopoeia and the reliability of the results depend, in part, upon the quality of the reagents used in the performance of the procedures. The reagents are defined in Appendices 7.3, 7.4 and 7.5 showing their nature, degree of purity and the strengths of the solutions to be made from them. The requirements set out in these Appendices are not intended to imply that the materials are suitable for use in medicine; reagents not covered by monographs in the Pharmacopoeia shall not be claimed to be of I.P. quality.

The abbreviations 'Sp' are employed for reagents defined in the Appendices for the Limit Tests for Heavy Metals and Lead.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Reference Substances and Standard Preparations

I.P. Reference Substances and Standard Preparations of antibiotics and other substances are authentic specimens that have been verified for suitability for use as comparison standards in some of the tests and assays of the Pharmacopoeia. The words 'I.P. Reference Substance' are abbreviated to 'R.S.' wherever mentioned in the monographs or in the appendices.

All I.P. Reference Substances and Standard Preparations are issued under the direction of the Ministry of Health & Family Welfare, Government of India. They are the official reference substances to be used in case of doubt or dispute. Laboratory working standards may be prepared for routine analysis, provided they are standardised at regular intervals with reference to those issued by the Ministry of Health & Family Welfare.

Solvents

Where the name of the solvent is not stated the term 'solution' implies a solution in water. Where the use of water is either specified or implied in tests and assays, for the preparation of reagents or as a diluent, water complying with the requirements of the monograph on Purified Water is to be used. The term 'distilled water' indicates Purified Water prepared by distillation.

For special kinds of water such as 'carbon dioxide-free water' see Appendix 7.4, General Reagents.

The term 'alcohol' means Alcohol of the Indian Pharmacopoeia which is ethanol (95 per cent v/v). Other dilutions of ethanol are indicated by the term 'alcohol' followed by a statement of the percentage by volume of ethanol required.

The term 'ethyl alcohol' means absolute alcohol or dehydrated alcohol and Ethyl Alcohol of the Indian Pharmacopoeia must be used.

Procedures

Assay and test procedures are provided for determining compliance with Pharmacopoeial standards of identity, strength, quality and purity. Although the tests and assays which have been described are official methods on which the standards of the Pharmacopoeia depend, the analyst is not precluded from employing alternative methods, including automated procedures and methods of micro-analysis, if he is satisfied that the method which he uses will give a result of equivalent accuracy. In the event of doubt or dispute, the methods of analysis of the Pharmacopoeia are alone authoritative.

In Assays, the quantity to be taken is indicated. The amount stated is approximate only, but the quantity actually used must be accurately weighed and it must not deviate by more than 10 per cent from that stated.

In Tests, the quantity to be taken is indicated. This quantity must be used unless any divergence can be taken into account in conducting the test and calculating the result. The quantity taken is accurately weighed or measured with the degree of precision indicated by the number of significant figures stated and the procedures applied in a correspondingly adequate manner.

In Assays and Tests of dosage forms not less than the specified number of dosage units should be taken for analysis. Proportionately

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

larger or smaller quantities than the specified weights and volumes of assay or test substances and Reference Standards or Standard Preparations may be taken, provided the measurement is made with at least equivalent accuracy and provided that any subsequent steps, such as dilutions, are adjusted accordingly to yield concentrations equivalent to those specified and are made in such a manner as to provide at least equivalent accuracy. Where it is directed in the assay of Tablets to "weigh and powder not less than" a given number of the Tablets, it is intended that a counted number of Tablets shall be weighed and reduced to a powder. Likewise, where it is directed in the assay of Capsules to weigh the mixed contents of a given number of the Capsules, it is intended that a counted number of Capsules are emptied and the contents thoroughly mixed. The portion of the powdered tablets or mixed contents of the capsules taken for assay is representative of the whole Tablets or Capsules respectively, and is, in turn, weighed accurately. The result of the assay is then related to the amount of active ingredient per tablet and in the case of Capsules, per capsule, from the weight of contents of each capsule.

Where the standards for a substance are defined in the monograph in terms of the chemical formula with reference to the dried or anhydrous or ignited substance, the directions for drying or igniting the sample prior to assaying are generally omitted from the Assay procedure. Assay and test procedures may be performed on the undried or unignited substance and the results calculated on the dried, anhydrous or ignited basis, provided a test for Loss on drying, or Water, or Loss on ignition, respectively, is given in the monograph.

Expressions such as 25.0 ml, 100.0 ml and 5.0 g, used with respect to volumetric or gravimetric measurements, indicate that the quantity is to be 'accurately measured' or 'accurately weighed' within the limits stated under 'Volumetric glassware' or under 'Weights and Balances'.

The term 'transfer' is used generally to indicate a quantitative operation.

Blank Determination

Where it is directed that 'any necessary correction' be made by a blank determination, the determination is to be done using the same quantities of the same reagents treated in the same manner as the solution or mixture containing the portion of the substance under assay or test, but omitting the substance being examined.

Dilution

Where it is directed that a solution be diluted 'quantitatively and stepwise', an accurately measured quantity is to be diluted by adding water or other solvent, in the proportion indicated, in one or more steps. The relatively larger errors associated with the use of small-volume volumetric apparatus must be borne in mind when carrying out dilutions.

Filtration

Where it is directed to filter, without further qualification, it is intended that the liquid be filtered through suitable filter paper or equivalent device until the filtrate is clear.

Identification Tests

The tests described under this sub-heading are not necessarily sufficient to establish absolute proof of identity. They provide a means of verify-

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

ing that the material being examined is in accordance with the label on the container.

The identification reactions of ions and groups of substances are brought together in an appendix instead of being frequently repeated in the monographs. In certain monographs more than one identification test has been given; compliance with these tests is necessary to verify the identity of the material.

When identification tests for infra-red absorption are applied to material extracted from dosage forms, strict concordance with the spectrum from the reference substance may not always be possible, but a close resemblance between the two spectra should be achieved.

Ignition to Constant Weight The specification 'ignite to constant weight' means that ignition shall be continued, at 800 ± 25°, unless otherwise indicated, until two consecutive weighings do not differ by more than 0.50 mg per g of substance taken, the second weighings being done after an additional ignition period of fifteen minutes.

Indicators Where the use of an indicator solution is specified in a test or assay, approximately 0.1 ml or three drops shall be added, unless otherwise directed.

Loss on Drying and Water Where absorbed water or water of hydration is determined by drying under specified conditions, the test is generally given under the heading 'Loss on drying'. It must, however, be understood that the loss in weight also represents residual volatile constituents including organic solvents as well as water. Where the determination is done by the titrimetric method, the test is generally given under the heading 'water'

Negligible The term 'negligible' indicates a quantity not exceeding 0.5 mg.

Pressure Measurements Pressure has been indicated in terms of 'mm of mercury' or 'Torr'. The term 'mm of mercury' used with respect to measurements of blood pressure (for example, in the test for histamine-like substances) or atmospheric pressure refers to the use of a suitable manometer or barometer calibrated in terms of the pressure exerted by a column of mercury of the stated height.

Temperature Unless otherwise specified, all temperatures in this Pharmacopoeia are expressed in Celsius (Centigrade) scale and all measurements are made at 25°

Normal Temperature and Pressure This refers to an atmospheric pressure of 760 Torr and a temperature of 0°

Time Limit In conducting the tests and assays, five minutes shall be allowed for the reaction to take place, unless otherwise specified.

Vacuum The term 'in vacuo' or 'in vacuum' denotes exposure to a pressure of less than 20 Torr, unless otherwise indicated.

Biological and Microbiological Tests and Assays Methods of biological and microbiological tests and assays are described in Appendices 2 and 4, respectively.

The methods of biological assay are provided for two purposes,

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

namely, to ascertain the purity of the material and to determine the total activity of the drug in a container. Monographs may require the assay to be carried out for one or both of these purposes.

When the assay is being used to ascertain the purity of the material, the stated potency means the potency stated on the label in terms of Units or micrograms per gram, Units or micrograms per milligram, or Units or micrograms per millilitre. When no such statement appears on the label, the stated potency means the fixed or minimum potency required in the monograph. This interpretation of stated potency applies in all cases except where the monograph specifically directs otherwise.

When the assay is being used to determine the total activity of the drug in the container, the stated potency means the total number of Units stated on the label or if no such statement appears, the total activity calculated in accordance with the instructions in the monograph.

Calculation of Results

The results of assays should be calculated to one decimal place more than indicated in the requirement and then rounded up or down as follows: if the last figure calculated is 5 to 9, the preceding figure is increased by 1; if it is 4 or less, the preceding figure is left unchanged. Other calculations are carried out similarly.

PACKAGING, STORAGE AND LABELLING

Containers : The container is the device that holds the article. The *immediate container* is that which is in direct contact with the article at all times. The *closure* is part of the container.

The container should not interact physically or chemically with the article placed in it so as to alter the strength, quality, or purity of the article beyond the official requirements.

Light-resistant Container : A light-resistant container protects the contents from the effects of light by virtue of the specific properties of the material of which it is made. Alternatively, a clear and colourless or a translucent container may be made light-resistant by means of an opaque covering; in such cases, the label of the container should bear a statement that the opaque covering is needed until the contents have been used up.

Well-closed Container : A well-closed container protects the contents from extraneous solids and from loss of the article under normal conditions of handling, shipment, storage and distribution.

Tightly-closed Container : A tightly-closed container protects the contents from contamination by extraneous liquids, solids or vapours, from loss of the article from effervescence, deliquescence or evaporation under normal conditions of handling, shipment, storage and distribution. A tightly-closed container must be capable of being tightly reclosed after use. Where a tightly-closed container is specified, a hermetically sealed container may be used for a single dose of an article.

A gas cylinder may be considered to be a metallic, tightly-closed container designed to hold gas under pressure.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Hermetically-sealed Container

A hermetically-sealed container is impervious to air or any other gas under normal conditions of handling, shipment, storage, and distribution.

Single-dose Container

A single-dose container is intended for articles for parenteral administration and is designed to hold a quantity of drug equivalent to a single dose.

Multiple-dose Container

A multiple-dose container is intended for articles for parenteral administration and is designed to permit withdrawal of successive portions of the contents without changing the strength, quality or purity of the remaining portion.

Containers for Ophthalmic Preparations

The containers or components of the immediate containers (e.g., nozzles, droppers, etc.) of a sterile article for ophthalmic use, except where compounded for immediate dispensing on prescription, should be so sealed that the contents and the components maintain sterility.

Storage

Storage conditions do not form a part of the 'Standards'; where, however, they are stated in some monographs, they are defined by the following terms:

Cold : Any temperature not exceeding 8° and usually between 2° and 8°.

Cool : Any temperature between 8° and 25°. An article for which storage in a cool place is directed may, alternatively, be stored in a refrigerator (at a temperature between 2° and 8°), unless otherwise specified in the individual monograph.

Room Temperature : The temperature prevailing in a working area.

Warm : Any temperature between 30° and 40°.

Excessive Heat : Any temperature above 40°.

Storage Under Non-specific Conditions : Where no specific directions are indicated in the individual monograph, it is to be understood that the storage conditions include protection from moisture, freezing and excessive heat.

Labelling

In general, the labelling of drugs and pharmaceuticals is governed by the Rules made under the Drugs and Cosmetics Act, 1940. In certain cases, additional information which must be stated on the label is specified in the monograph.

Weights and Measures

The metric system of weights and measures is employed in the Pharmacopoeia. All measures are required to be graduated at 25°

When the term 'drop' is used, the measurement is to be made by means of a tube which delivers 20 drops per g of Purified Water at 15°

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

ABBREVIATIONS

The abbreviations commonly employed are as follows:

$[\alpha]_D^{20}$	=	Specific optical rotation
bp	=	Boiling point
cm	=	Centimetre
dl	=	Decilitre
dm	=	Decimetre
g	=	Gram
I.U.	=	International Unit
kg	=	Kilogram
LD_{50}	=	Lethal dose 50 (the dose of a preparation or organism which kills 50 per cent of the animals inoculated)
l	=	Litre
mp	=	Melting point
mEq	=	Milliequivalent
mmol	=	Millimole
µl	=	Microlitre
µg	=	Microgram (formerly the abbreviation 'mcg' was used)
µm	=	Micrometre (0.001 mm)
mg	=	Milligram
ml	=	Millilitre [used as the equivalent to cubic centimetre (cc)]
mm	=	Millimetre
mV	=	Millivolt
mol	=	Gram-molecular weight (mole)
ng	=	Nanogram
nm	=	Nanometre [formerly the abbreviation 'mµ' (for millimicron) was used]
ppm	=	Parts by weight per million
psi	=	Pounds per square inch
P.S.	=	Primary Standard
rpm	=	Revolutions per minute
R.S.	=	I.P. Reference Substance
Sp. gr.	=	Specific gravity
Wt. per ml	=	Weight per millilitre

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Monographs

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Acacia

Gum Acacia, Indian Gum

Category : Pharmaceutical aid (emulsifying and suspending agent).

Description : Irregular and broken pieces (tears) of varying size, yellowish-white, yellow or amber in colour, with numerous minute fissures, brittle fractured surface, glassy and occasionally iridescent. Odourless; taste, bland and mucilaginous.

Solubility : Almost entirely soluble in twice its weight of *water* yielding a very viscous, slightly acid solution which is slightly glairy and when diluted with more *water* and allowed to stand, yields a very small amount of gummy deposit; practically insoluble in *alcohol*.

Standards : Indian Gum is the dried, gummy exudation from the stem and branches of *Acacia nilotica* (Linn.) Del. subsp. *indica* (Benth.) Brenan (syn. *A. arabica* Willd. var. *indica* Benth.) (Fam. Leguminosae), or other species of *Acacia*.

Identification : (A) An aqueous solution is gelatinised by the addition of *lead subacetate solution*.

(B) When examined microscopically the powder does not acquire a pink colour with *ruthenium red solution* (distinction from sterculia gum and from agar).

(C) To 5ml of a 10 per cent w/v solution add gradually, while shaking, 10 ml of *alcohol*. The cloudy liquid, on addition of 0.5 ml of *acetic acid*, gives a white precipitate. Filter and add to the clear filtrate 50 ml of *ammonium oxalate solution*; the filtrate becomes cloudy.

(D) A 10 per cent w/v solution is either dextrorotatory or slightly laevorotatory.

Agar and tragacanth; Starch and dextrin; Tannins; Sucrose and fructose : A 10 per cent w/v solution complies with the following tests:

Agar and tragacanth : To 10 ml add 0.2 ml of *lead acetate solution*; no precipitate is produced.

Starch and dextrin : Boil 10 ml and cool, add 0.1 ml of *0.1N iodine*; no blue or brown colour is produced.

Tannins : To 10 ml add 0.1 ml of *ferric chloride test-solution*; a gelatinous precipitate is formed, but neither the precipitate nor the liquid shows a dark blue colour.

Sucrose and fructose : To 1 ml add 4 ml of *water*, 0.1 g of *resorcinol* and 2 ml of *hydrochloric acid* and heat on a water-bath; no yellow or pink colour develops.

Insoluble matter : Dissolve 5 g of fine powder in about 100 ml of *water* in a 250-ml Erlenmeyer flask; add 10 ml of *dilute hydrochloric acid* and boil gently for fifteen minutes. Filter by suction while hot, through a sintered-glass crucible, previously tared, wash thoroughly with hot water, dry at 105° and weigh; the residue does not exceed 50 mg.

Sulphated ash : Not more than 5.0 per cent, calculated with reference to the dried substance, Appendix 3.2.7.

Acid-insoluble ash : Not more than 1.0 per cent, Appendix 3.3.22.

Loss on drying : Not more than 15.0 per cent, determined on 0.5 g by drying in an oven at 105°, Appendix 5.8.

Storage : Store in tightly-closed containers, protected from moisture.

ACACIA POWDER

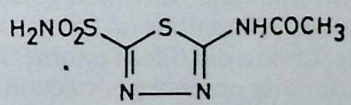
Description : White or yellowish-white powder; odourless and tasteless; on treatment with *water* it dissolves to give a mucilaginous liquid which is colourless or yellowish, dense, viscous, adhesive and translucent.

Solubility ; Identification; Agar and tragacanth; Starch and dextrin; Tannins; Sucrose and fructose; Water-insoluble matter; Sulphated ash; Acid-insoluble ash; Loss on drying: complies with the requirements stated under Acacia.

Microbial limits : 1.0 g is free from *E. coli*, Appendix 4.5.

Storage : Store in tightly-closed containers, protected from moisture.

Acetazolamide



$C_4H_6N_4O_3S_2$ Mol. Wt. 222.24

Category : Carbonic anhydrase inhibitor.

Dose : Initial dose 0.5 g; subsequent doses, 0.25 g every six hours.

Description : White or yellowish-white, crystalline powder; odourless; tasteless.

Solubility : Very slightly soluble in *water*; slightly soluble in *alcohol*; practically insoluble in *chloroform* and in *solvent ether*.

Standards : Acetazolamide is *N*-(5-sulphamoyl-1,

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

3,4-thiadiazol-2-yl) acetamide. It contains not less than 98.0 per cent and not more than 102.0 per cent of $C_4H_6N_4O_3S_2$, calculated with reference to the anhydrous substance.

Identification : (A) Triturate about 0.5 g with 5 ml of *water*, made alkaline with 1 ml of *N sodium hydroxide*; add about 0.2 g of *zinc powder* and 0.5 ml of *hydrochloric acid*, mix well; hydrogen sulphide evolved is recognised by its characteristic odour.

(B) To about 25 mg add 5 ml of *water*, 4 drops of *N sodium hydroxide* and 2 drops of *copper sulphate solution*; a bluish-green colour or precipitate is produced.

Light absorption : Weigh accurately about 0.2 g and dissolve in 200 ml of boiling *water*, dilute to 900 ml with *water*, cool, and add sufficient *water* to produce 1000.0 ml. To 5.0 ml add 10 ml of *N hydrochloric acid* and sufficient *water* to produce 100.0 ml. *Extinction* of a 1-cm layer of the resulting solution at the maximum at about 265 nm, 0.46 to 0.49, Appendix 5.15A.

Silver-precipitating substances : Mix 5 g with 25 ml of *alcohol*, add 125 ml of *water*, 10 ml of *nitric acid*, and 5 ml of *0.1 N silver nitrate*, stir for thirty minutes; filter, wash the residue with *water*, and titrate the excess of silver nitrate in the combined filtrate and washings with *0.05 N ammonium thiocyanate*, using *ferric ammonium sulphate solution* as indicator; not less than 9.5 ml of *0.05 N ammonium thiocyanate* is required.

Heavy metals : Not more than 20 parts per million, determined by Method C, on 1.0 g dissolved in a mixture of 10 ml of *N sodium hydroxide* and 15 ml of *water*, Appendix 3.2.4.

Water : Not more than 0.5 per cent w/w, Appendix 3.3.25.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Assay : Weigh accurately about 0.4 g and dissolve in 90 ml of *dimethylformamide*. Titrate with *0.1 N tetrabutylammonium hydroxide*, determining the end-point potentiometrically and taking precautions to prevent absorption of atmospheric carbon-dioxide. Perform a blank determination and make any necessary correction. Each ml of *0.1 N tetrabutylammonium hydroxide* is equivalent to 0.02222 g of $C_4H_6N_4O_3S_2$.

Storage : Store in well-closed containers.

Acetazolamide Tablets

Category : Carbonic anhydrase inhibitor.

Dose : Acetazolamide, initial dose 0.5 g; subsequent doses, 0.25 g every six hours.

Usual strength : 0.25 g.

Standards : Acetazolamide Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Acetazolamide, $C_4H_6N_4O_3S_2$.

Identification : The powdered tablets comply with **Identification** tests (A) and (B) described under Acetazolamide.

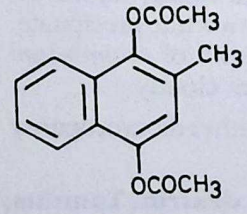
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 0.2 g of Acetazolamide, add 500 ml of *water* and heat on a water-bath for fifteen minutes with occasional shaking. Cool, and add sufficient *water* to produce 1000.0 ml. Mix well and filter. To 10.0 ml of the filtrate add 25 ml of *N hydrochloric acid* and sufficient *water* to produce 250.0 ml. Measure the *extinction* of 1-cm layer of the resulting solution at the maximum at about 265 nm, Appendix 5.15A. Calculate the content of $C_4H_6N_4O_3S_2$ from the *extinction* obtained by repeating the operation using *acetazolamide R.S.* instead of the substance being examined.

Storage: Store in well-closed containers.

Acetomenaphthone

Acetomenadione



$C_{15}H_{14}O_4$ Mol. Wt. 258.27

Category : Prothrombogenic Vitamin (Vitamin K substitute).

Dose : In the prophylaxis of neonatal haemorrhage, 5 to 10 mg daily for one week before delivery.

In the pre-operative treatment of obstructive jaundice, 10 to 20 mg daily for one week.

In haemorrhagic disease of the new born, a total of 1 mg over a period of twenty-four hours; for premature babies, a total of 0.5 mg over a period of twenty-four hours.

Description : White, crystalline powder; odourless or with a slight odour of acetic acid; taste, bitter.

Solubility : Practically insoluble in *water*; slightly

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

soluble in cold *alcohol*; freely soluble in boiling *alcohol*.

Standards : Acetomenaphthone is 1,4-diacetoxy-2-methylnaphthalene. It contains not less than 98.0 per cent and not more than 101.0 per cent of $C_{15}H_{14}O_4$, calculated with reference to the dried substance.

Identification : (A) The light absorption in the range 230 to 350 nm, of a 1-cm layer of a 0.002 per cent w/v solution in *ethyl alcohol* exhibits two maxima, at 285 nm and 322 nm; *extinction* at 285 nm, about 0.5, and at 322 nm, about 0.075, Appendix 5.15A.

(B) It gives the reactions of *acetyl groups*, Appendix 3.1.

Melting range : Between 112° and 115°, Appendix 5.11.

Zinc : Heat 1.0 g with 10 ml of *dilute hydrochloric acid*, filter, and wash the residue with sufficient hot *water* to yield 50 ml of filtrate; add 1 ml of *potassium ferrocyanide solution*; the turbidity produced is not greater than that produced by adding 1 ml of *potassium ferrocyanide solution* to a solution of 0.2 mg of *zinc sulphate* in 40 ml of *water* and 10 ml of *dilute hydrochloric acid*.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 80°, Appendix 5.8.

Assay : Weigh accurately about 0.2 g and boil with 15 ml of *glacial acetic acid* and 15 ml of *dilute hydrochloric acid* under a reflux condenser for fifteen minutes. Cool, taking precautions to avoid air oxidation, and titrate with *0.05N ceric ammonium sulphate*, using 0.1 ml of *ferroin sulphate solution* as indicator. Repeat the operation without the substance being examined. Each ml of *0.05 N ceric ammonium sulphate* is equivalent to 0.006457 g of $C_{15}H_{14}O_4$.

Storage : Store in well-closed containers.

Acetomenaphthone Tablets

Acetomenadione Tablets

Category : Prothrombogenic Vitamin (Vitamin K substitute).

Dose : Acetomenaphthone. In the prophylaxis of neonatal haemorrhage, 5 to 10 mg daily for one week before delivery.

In the pre-operative treatment of obstructive jaundice 10 to 20 mg daily for one week. In the haemorrhagic disease of the new born, a total of 1 mg over a period of twenty-four hours; for premature babies, a total of 0.5 mg over a period of twenty-four hours.

Usual strengths : 1 mg; 5 mg.

Standards: Acetomenaphthone Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Acetomenaphthone, $C_{15}H_{14}O_4$. The tablets may be coated.

Identification : Boil a quantity of the powdered tablets equivalent to about 0.1 g of Acetomenaphthone with 5 ml of *alcohol*, and filter quickly. Boil with a further 5 ml of *alcohol*, and filter. Evaporate the alcohol on a water-bath; the residue complies with **Identification** test (A) described under Acetomenaphthone.

Uniformity of content : Crush one tablet, add 25 ml of *ethyl alcohol*, shake for fifteen minutes. Add sufficient *ethyl alcohol* to produce 50.0 ml and centrifuge. If necessary dilute a suitable volume of the clear supernatant liquid with *ethyl alcohol* to produce a solution containing about 0.002 per cent w/v of Acetomenaphthone. Measure the *extinction* of the resulting solution at the maximum at about 285 nm, Appendix 5.15A. Calculate the content of $C_{15}H_{14}O_4$, taking 250 as the value of E(1 per cent, 1-cm) at the maximum at about 285 nm.

Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 90 per cent and 110 per cent, of the average except for one tablet, the content may be between 85 per cent and 115 per cent of the average.

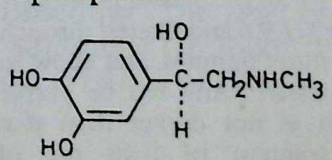
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets, or more if necessary. Weigh accurately a quantity of the powder equivalent to about 0.2 g of Acetomenaphthone and extract in a continuous extraction apparatus with *chloroform* for two hours. Remove the chloroform, add 15 ml of *glacial acetic acid* and 15 ml of *dilute hydrochloric acid*, boil under a reflux condenser for fifteen minutes, and complete the **Assay** described under Acetomenaphthone, beginning at the words "Cool, taking precautions.....".

Storage : Store in tightly-closed containers.

Adrenaline

Epinephrine



$C_9H_{13}NO_3$ Mol. Wt. 183.21

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Category : Adrenergic.

Dose : By subcutaneous or intramuscular injection, 0.2 to 0.5 mg, as a single dose.

Description : White or creamy-white, micro-crystalline powder or granules. It gradually darkens on exposure to light and air.

Solubility : Sparingly soluble in *water*; insoluble in *alcohol* and in *solvent ether*; soluble in solutions of mineral acids, of *sodium hydroxide*, and of *potassium hydroxide*, but not in solutions of ammonia and of the alkali carbonates.

It is not stable in a neutral or alkaline solution, which rapidly becomes red on exposure to air.

Standards : Adrenaline is (*R*)-1-(3,4-dihydroxyphenyl)-2-methylaminoethanol. It contains not less than 97.0 per cent and not more than the equivalent of 101.0 per cent of $C_9H_{13}NO_3$, calculated with reference to the dried substance.

Identification : (A) To a neutral or faintly acid solution, add a 0.25 per cent w/v solution of *ferric chloride*; an emerald green colour develops which, on the gradual addition of *sodium bicarbonate solution*, changes first to blue and then to red.

(B) It melts at about 212°, with decomposition, the rate of rise of temperature being 10° per minute, Appendix 5.11.

(C) The light absorption in the range 230 to 350 nm, of a 1-cm layer of a 0.003 per cent w/v solution in *0.01N hydrochloric acid* exhibits a maximum only at 280 nm; *extinction* at 280 nm, about 0.45, Appendix 5.15A.

Specific optical rotation : Between −50° and −53.5°, calculated with reference to the dried substance and determined in a freshly prepared 4.0 per cent w/v solution in *N hydrochloric acid*, Appendix 5.12.

Phenones : *Extinction* of a 1-cm layer of a 0.2 per cent w/v solution in *0.01N hydrochloric acid* at 310 nm, not greater than 0.2, Appendix 5.15A.

Noradrenaline : Dissolve 5.0 mg in 1 ml of a 0.5 per cent w/v solution of *tartaric acid*, add 4 ml of *buffer solution pH 9.6*, mix, add 1 ml of freshly prepared 0.5 per cent w/v solution of *sodium 1, 2-naphthaquinone-4-sulphonate*, mix and allow to stand for thirty minutes. Add 0.2 ml of a 1 per cent v/v solution of *benzalkonium chloride solution*, mix, add 15 ml of *toluene* previously washed with *buffer solution pH 9.6* and filtered through a dry filter paper, shake for thirty minutes, and allow to separate, centrifuging if necessary. Any red or purple colour in the toluene layer is not darker than that produced by treating a solution of 0.40 mg of *noradrenaline acid tartrate* and 9 mg of *noradrenaline-free adrenaline acid tartrate* in 1 ml of *water* in a similar manner.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

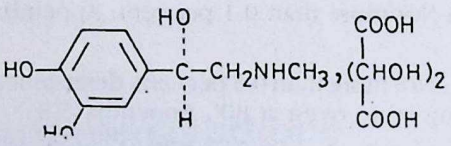
Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying "in vacuo" for eighteen hours, Appendix 5.8.

Assay : Weigh accurately about 0.3 g and dissolve in 50 ml of *glacial acetic acid*, warming slightly if necessary to effect solution. Cool, add *crystal-violet solution* and titrate with *0.1N perchloric acid* to a bluish-green end-point. Perform a black determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.01832 g of $C_9H_{13}NO_3$.

Storage : Store in tightly-closed, light-resistant containers, preferably filled with nitrogen.

Adrenaline Bitartrate

Adrenaline Acid Tartrate; Epinephrine Bitartrate



$C_9H_{13}NO_3, C_4H_6O_6$ Mol. Wt. 333.29

Category : Adrenergic.

Dose : By subcutaneous injection, 0.4 to 1 mg as a single dose.

Description : White or greyish-white, or light brownish-grey, crystalline powder; odourless. It darkens on exposure to air and light.

Solubility : Freely soluble in *water*; slightly soluble in *alcohol*; practically insoluble in *chloroform* and in *solvent ether*.

Standards : Adrenaline Bitartrate is (*R*) – (β,3,4-trihydroxyphenethyl) methylammonium hydrogen tartrate. It contains not less than 97.0 per cent and not more than the equivalent of 102.0 per cent of $C_9H_{13}NO_3$, $C_4H_6O_6$, calculated with reference to the dried substance.

Identification : (A) Dissolve 0.3 g in 10 ml of *water* containing 0.1 g of *sodium metabisulphite*, add a slight excess of *dilute ammonia solution* and allow to stand at about 4° for one hour. Filter, wash the precipitate with three successive quantities, each of 2 ml, of cold *water*, then with 5 ml of cold *alcohol* and finally with 5 ml of cold *solvent ether* and dry "in vacuo" over *silica gel* for

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

R 615.19 END-P.I.2

पुस्तकालय

three hours. The residue complies with the **Identification** test (A) described under Adrenaline, and has a *specific optical rotation*, in a 4 per cent w/v solution in *N hydrochloric acid*, of about −52°, Appendix 5.12.

(B) The filtrate obtained in **Identification** test (A) gives the reactions of *tartrates*, Appendix 3.1.

(C) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.005 per cent w/v solution in *0.01N hydrochloric acid* exhibits a miximum only at 279 nm; *extinction* at 279 nm, about 0.4, Appendix 5.15A.

(D) It melts at about 150° with decomposition, Appendix 5.11.

pH : Between 2.8 and 4.0, determined in a 1.0 per cent w/v solution, Appendix 5.10.

Adrenalone : *Extinction* of a 1-cm layer of a 0.1 per cent w/v solution in *0.01N hydrochloric acid* at 310 nm, not greater than 0.2, Appendix 5.15 A.

Noradrenaline : Dissolve 10.0 mg in 1.0 ml of *water* in a 25-ml glass-stoppered cylinder and complete the test for **Noradrenaline** described under Adrenaline, beginning at the words "add 4.0 ml of *buffer solution pH 9.6*....."

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying "in vacuo" for eighteen hours, Appendix 5.8.

Assay : Carry out the **Assay** described under Adrenaline. Each ml of *0.1N perchloric acid* is equivalent to 0.03333 g of $C_9H_{13}NO_3$, $C_4H_6O_6$.

Storage : Store in tightly-closed, light-resistant containers, preferably filled with nitrogen.

108834

Adrenaline Tartrate Injection

Adrenaline Injection; Epinephrine Tartrate Injection

Category : Adrenergic.

Dose : By subcutaneous injection, 0.2 to 0.5 ml as a single dose. In the treatment of status asthmaticus and other allergic emergencies, by subcutaneous injection, 0.05 ml per minute.

By intravenous injection, 0.1 to 0.25 ml, diluted to 0.3 to 2.5 ml with Water for Injection.

Description : Clear, colourless or nearly colourless solution.

Standards : Adrenaline Tartrate Injection contains the equivalent of not less than 0.09 per cent and not more than 0.115 per cent w/v of Adrenaline, $C_9H_{13}NO_3$.

Adrenaline Bitartrate	0.18 g
Sodium Metabisulphite	0.1 g
Sodium Chloride	0.8 g
Water for Injection, sufficient to produce	100 ml

Dissolve the Sodium Metabisulphite in 10 ml of Water for Injection and add the Adrenaline Bitartrate. Dissolve the Sodium Chloride in 75 ml of Water for Injection. Mix the two solutions and add sufficient Water for Injection to produce 100 ml. Sterilise.

pH : Between 2.8 and 3.6, Appendix 5.10.

Other requirements : Complies with the requirements stated under Injections.

Assay : Extract 30.0 ml in a separator with three quantities, each of 25 ml, of *carbon tetrachloride*, shaking vigorously for one minute each time; reject the carbon tetrachloride extracts. Add 0.2 ml of *starch solution* and, dropwise with swirling, a solution prepared by dissolving 0.5 g of *iodine* and 1.5 g of *potassium iodide* in 25 ml of *water*, until the blue colour persists. Immediately add just sufficient *0.1N sodium thiosulphate* to discharge the blue colour and proceed with the assay from this point without delay. Add 2.10 g of *sodium bicarbonate* and swirl until most of the sodium bicarbonate has dissolved. Using a syringe, rapidly inject 1.0 ml of *acetic anhydride* directly into the contents of the separator, insert the stopper, and shake vigorously until the evolution of carbon dioxide ceases (seven to ten minutes), releasing the pressure when necessary through the stop-cock. Allow to stand for five minutes and extract with six successive quantities, each of 25 ml, of *chloroform*, filtering each extract into a beaker through a small plug of cotton wool moistened with *chloroform*. Remove the chloroform, heat the residue at 105° for thirty minutes, allow to cool, and weigh. Dissolve the residue in 5.0 ml of *chloroform* swirling to assist solution, and determine the *specific optical rotation* of the resulting solution, Appendix 5.12, using a 2-dm tube. Calculate the percentage w/v of adrenaline, $C_9H_{13}NO_3$, in the injection from the expression:

$$1.974W(0.5 + 0.5\ R/93)$$

Where W is the weight of residue in g and R is its *specific optical rotation* (in degrees without regard to the sign).

Storage : Store in single-dose or multi-dose, light-resistant containers.

Labelling : The label on the container states (1) 'Adrenaline 1 in 1000'; (2) 'Do not use the Injection if it is brown or contains a precipitate'.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Human Normal Serum Albumin

Human Albumin

Category : Blood-volume supporter.

Dose : By intravenous injection, volume equivalent to 25 g of albumin.

Description : Clear liquid, ranging in colour from amber to deep orange-brown with increasing protein concentration; almost odourless.

Standards : Human Normal Serum Albumin is a sterile non-pyrogenic solution of the albumin component of human blood containing a low proportion of salt. It is obtained by fractionating source materials such as blood, plasma, serum or placentas from healthy human donors and tested for the absence of hepatitis B surface antigen. It may be prepared from pooled source materials by precipitation with organic solvents under controlled conditions of pH, ionic strength and temperature or by any other method which shall not affect the integrity of the product and shall have been shown to yield consistently a product which is safe for intravenous injection. Residual solvent, if present, is removed by freeze-drying or other suitable treatment. The product is dissolved in water, and at pH 7.0 a suitable stabilising agent is added to stabilise it to heat. No bactericide or antibiotic is added at any stage during preparation and all processing steps are conducted in a manner to minimise risk of contamination from either micro-organisms or other deleterious matter. The solution is sterilised by *Filtration* and distributed aseptically into containers, which are then sealed so as to exclude micro-organisms. The solution is then heated to and maintained at 59.5° to 60.5° for ten hours so as to prevent the transmission of serum hepatitis. Finally, the containers are stored for not less than 14 days at 30° to 32° and examined visually. Those showing abnormalities such as abnormal colour, turbidity, microbial contamination, or presence of atypical particles shall be discarded.

Human Normal Serum Albumin contains not less than 5.0 per cent and not more than 25.0 per cent w/v of protein, and not more than 0.65 millimole of sodium ions, and 0.05 millimoles of potassium per g of protein.

Identification : (A) By precipitation tests with specific antisera, contains plasma proteins of human origin only.

(B) By *electrophoresis*, using the moving boundary technique, in a buffer of barbitone and its sodium salt at pH 8.6 and ionic strength 0.1, 96 per cent of the protein has the mobility of human albumin, Appendix 5.9.

pH : Between 6.5 and 7.5, Appendix 5.10.

Haem content : Dilute with sufficient of a 0.9 per cent w/v solution of *sodium chloride* to produce a solution containing 1.0 per cent w/v of protein; the *extinction* of a 1-cm layer of the resulting solution at 403 nm, is not more than 0.25, Appendix 5.15A

Denatured protein : Equilibrate a column, 60 to 75 cm long and 2.5 to 3.0 cm in diameter, of a gel of a cross-linked dextran suitable for fractionation of proteins in the range of molecular weight from 5000 to 150,000 with a lower molecular weight for complete exclusion of globulin proteins between 400,000 and 500,000 (Sephadex G 150 is suitable) at 20° to 25° with a saline-phosphate solution prepared by mixing 2 volumes of a 0.88 per cent w/v solution of *sodium chloride* and 1 volume of sodium phosphate buffer, pH 7.0, ionic strength 0.15. Apply to the column 2.5 ml of normal human serum, previously clarified by centrifuging, and elute with the saline-phosphate solution at a rate of 25 ml per hour. Prepare a chromatogram by recording the *extinction*, Appendix 5.15 A, of the eluate at 280 nm in relation to its volume. The chromatogram exhibits three well-defined peaks. Determine the volume, V, of the eluate from the entry of the sample into the column to the apex of the first peak.

Dilute the substance being examined with the saline-phosphate solution to contain about 5 per cent w/v of protein, apply 2.5 ml to the column, and elute under the same conditions, collecting the eluate in 5 ml portions. Three peaks may appear in similar positions to those in the chromatogram obtained from the serum but the relative peak heights may be different. To the fraction eluted between volume 0.85 V and 1.15 V, add for each 10 ml, 0.4 ml of a 7.5 per cent w/v solution of *sodium molybdate* and 0.4 ml of a mixture of 1 part of *nitrogen-free sulphuric acid* and 30 parts of *water*, shake, centrifuge for five minutes, and complete the **Assay** described under Human Plasma, beginning at the words "decant the supernatant.. ...". The weight of protein in the fraction of the eluate is not more than 3.5 per cent of the weight of protein in the volume of the substance being examined applied to the column.

Heat the substance being examined for fifty hours at 56.5° to 57.5° and repeat the chromatographic separation and the determination of the weight of protein in the fraction eluted between 0.85 V and 1.15 V. When expressed as a percentage of the weight of protein in the volume of the substance being examined applied to the column, it exceeds the percentage obtained before heating by not more than 1.5 per cent w/v.

Stability : The contents of the final container remain unchanged, as determined by visual inspection, after heating at 57° for 50 hours, when compared to its control

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

consisting of a sample from the same lot, which has not undergone this heating.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using a volume containing 0.5 g of protein per kg of the rabbit's weight and rabbits that have not previously received blood products.

Sterility : Complies with the *tests for sterility*, Appendix 4.6, using sample taken from the final container drawn at random prior to the heating procedure at 60° for 10 hours.

Undue toxicity : Complies with the *test for undue toxicity for vaccines and sera*, Appendix 2.37, using 0.5 ml of the solution for each mouse and 5 ml for each guinea-pig.

Assay : (1) *For protein* – Dilute with *water* to contain about 5 per cent w/v of protein and carry out the **Assay** described under Normal Human Plasma, using 0.2 ml.

(2) *For sodium ions* – Dilute to 0.01 per cent w/v of protein with *water* and determine by Method B for *flame photometry*, Appendix 5.16, measuring at 589 nm and using *sodium solution FP* suitably diluted with *water* as the standard solution.

(3) *For potassium ions* – Dilute to 0.25 per cent w/v of protein with *water* and determine by Method B for *flame photometry*, Appendix 5.16, measuring at 767 nm and using *potassium solution FP* suitably diluted with *water* as the standard solution.

Storage : Store at a temperature between 2° and 25° and protect from light.

Labelling : The label on the container states (1) the volume; (2) the total amount of protein; (3) the concentration of sodium and potassium ions; (4) the names and concentrations of any stabilising agents added; (5) the type of source material used to manufacture the product; (6) the words "do not use if turbid or more than 4 hours after the container has been entered"; (7) the storage conditions; (8) the date after which the solution is not intended to be used.

Alcohol

Category : Pharmaceutical aid (solvent); topical anti-infective.

Description : Clear, colourless, mobile, volatile liquid; odour, characteristic and spirituous; taste, burning. Is readily volatilised even at low temperature, and boils at about 78° . Is flammable.

Solubility : Miscible in all proportions with *water*, with *chloroform* and with *solvent ether*.

Standards : Alcohol is a mixture of Ethyl Alcohol and Water. It contains not less than 92.0 per cent and not more than 92.7 per cent by weight, corresponding to not less than 94.7 per cent and not more than 95.2 per cent, by volume, at 15.56°, of C_2H_6O.

Identification : (A) Mix 5 drops in a small beaker with 1 ml of *potassium permanganate solution* and 5 drops of *dilute sulphuric acid* and cover the beaker immediately with a filter paper moistened with a solution recently prepared by dissolving 0.1 g of *sodium nitroprusside* and 0.5 g of *piperazine hydrate* in 5 ml of *water*; an intense blue colour is produced on the filter paper, the colour becoming paler after a few minutes.

(B) To 5 ml of a 0.5 per cent solution, add 1 ml of *N sodium hydroxide*; then slowly add 2 ml of *iodine solution*; the odour of iodoform develops and a yellow precipitate is produced.

Acidity or Alkalinity : To 20 ml add five drops of *phenolphthalein solution*; the solution remains colourless and requires not more than 0.2 ml of *0.1N sodium hydroxide* to produce a pink colour.

Specific gravity : Between 0.8084 and 0.8104 at 25°, Appendix 5.19.

Clarity of solution : Dilute 5 ml to 100 ml with *water* in a glass cylinder; the solution remains clear when examined against a black background. Cool to 10° for thirty minutes; the solution remains clear.

Methanol : To one drop add one drop of *water*, one drop of *dilute phosphoric acid*, and one drop of *potassium permanganate solution*. Mix, allow to stand for one minute and add *sodium bisulphite solution* dropwise, until the permanganate colour is discharged. If a brown colour remains, add one drop of *dilute phosphoric acid*. To the colourless solution add 5 ml of freshly prepared *chromotropic acid solution* and heat on a water-bath at 60° for ten minutes; no violet colour is produced.

Foreign organic substances : Clean a glass-stoppered cylinder thoroughly with *hydrochloric acid*, rinse with *water* and finally rinse with the alcohol under examination. Put 20 ml in the cylinder, cool to about 15° and then add from a carefully cleaned pipette 0.1 ml of *0.1N potassium permanganate*. Mix at once by inverting the stoppered cylinder and allow to stand at 15° for five minutes; the pink colour does not entirely disappear.

Isopropyl alcohol and *t*-butyl alcohol : To 1 ml add 3 ml of *water*, and 10 ml of *mercuric sulphate solution* and heat in a boiling water-bath; no precipitate is formed within three minutes.

Aldehydes and ketones : Heat 100 ml of *hydroxylamine hydrochloride solution* in a loosely stoppered flask on a water-bath for thirty minutes, cool, and, if necessary, add sufficient *0.05N sodium hydroxide* to restore the green colour. To 50 ml of this solution add

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

25 ml of the alcohol and heat on a water-bath for ten minutes in a loosely stoppered flask. Cool, transfer to a Nessler cylinder, and titrate with *0.05N sodium hydroxide* until the colour matches that of the remainder of the hydroxylamine hydrochloride solution contained in a similar cylinder, both solutions being viewed down the axis of the cylinder. Not more than 0.9 ml of *0.05N sodium hydroxide* is required.

Fusel oil constituents : Mix 10 ml with 5 ml of *water* and 1 ml of *glycerin* and allow the mixture to evaporate spontaneously from clean, odourless absorbent paper; no foreign odour is perceptible at any stage of the evaporation.

Non-volatile matter : Evaporate 40 ml in a tared dish on a water-bath and dry the residue at 105° for one hour; the weight of the residue does not exceed 1 mg.

Storage : Store in tightly-closed containers, away from fire.

Labelling : The label on the container states "Flammable".

Ethyl Alcohol

Absolute Alcohol; Dehydrated Alcohol

C_2H_6O Mol. Wt. 46.07

Category : Pharmaceutical aid (solvent).

Description : Clear, colourless, mobile, volatile liquid; odour, characteristic and spirituous; taste, burning; hygroscopic. Readily volatilises even at low temperature and boils at 78° . Is flammable.

Solubility : Miscible with *water*, with *solvent ether*, and with *chloroform*.

Standards : Ethyl Alcohol contains not less than 99.0 per cent and not more than 100.0 per cent by weight, corresponding to not less than 99.4 per cent and not more than 100.0 per cent by volume, at 15.56°, of C_2H_6O.

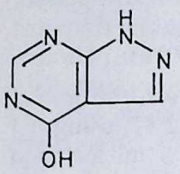
Identification; Acidity or Alkalinity; Clarity of solution; Methanol; Foreign organic substances; Isopropyl alcohol and *t*-butyl alcohol; Aldehydes and ketones; Fusel oil constituents; Non-volatile matter: Complies with the requirements described under Alcohol.

Specific gravity : Between 0.7871 and 0.7902, at 25°, Appendix 5.19.

Storage : Store in tightly-closed containers, in a cool place away from fire and protected from moisture.

Labelling : The label on the container states "Flammable".

Allopurinol



$C_5H_4N_4O$ Mol. Wt. 136.11

Category : Gout suppressant.

Dose : 200 to 400 mg daily, in divided doses.

Description : White or almost white, microcrystalline powder; odourless; tasteless.

Solubility : Very slightly soluble in *water* and in *alcohol*; practically insoluble in *chloroform* and in *solvent ether*; soluble in solutions of alkali hydroxides.

Standards : Allopurinol is 1*H*-pyrazolo (3, 4-*d*) pyrimidine-4-ol. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_5H_4N_4O$, calculated with reference to the dried substance.

Identification : (A) Shake about 0.1 g with 5 ml of *dilute sodium hydroxide solution*, add 3 ml of *lithium and sodium molybdophosphotungstate solution* and 5 ml of a 20 per cent w/v solution of *sodium carbonate*; a grey-blue colour is produced.

(B) Dissolve 50 mg in 5 ml of *dilute sodium hydroxide solution*; and 1 ml of *alkaline potassium mercuri-iodide solution*, heat to boiling and allow to stand; a flocculent yellow precipitate is produced.

(C) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of the solution prepared as described in the test for **Light absorption** exhibits a maximum only at 250 nm; *extinction* at 250 nm; about 0.55, Appendix 5.15 A.

Light absorption : Dissolve 0.10 g in 10 ml of *0.1N sodium hydroxide* and add sufficient *0.1N hydrochloric acid* to produce 100 ml; dilute 10 ml to 100 ml with *0.1N hydrochloric acid* and dilute 10 ml of this solution to 100 ml with *0.1N hydrochloric acid*. Ratio of the *extinction* of a 1-cm layer of the resulting solution at the minimum at about 231 nm to that at the maximum at about 250 nm, 0.52 to 0.60, Appendix 5.15A.

Related compounds : Carry out the method for *thin-layer chromatography*. Appendix 5.4.3, using a suitable cellulose powder containing a fluorescent additive as the

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

coating substance and *n-butyl alcohol* saturated with *dilute ammonia solution* as the mobile phase. Apply separately to the plate 10 µl of each of two freshly prepared solutions in a 10 per cent v/v solution of *diethylamine* containing (1) 2.5 per cent w/v of the substance being examined and (2) 0.0025 per cent w/v *3-aminopyrazole-4-carboxamide hemisulphate R.S.* After removal of the plate, allow it to dry in air and examine under an ultra-violet lamp having a maximum output of about 250 nm. Any spot in the chromatogram obtained with solution (1), other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (2).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.2 g, dissolve in 50 ml of *dimethylformamide* and titrate with *0.1N sodium methoxide* using a 0.3 per cent w/v solution of *thymol blue in methyl alcohol* as indicator and protecting the solution from atmospheric carbon dioxide throughout the titration. Each ml of *0.1N sodium methoxide* is equivalent to 0.01361 g of $C_5H_4N_4O$.

Storage : Store in well-closed containers.

Allopurinol Tablets

Category : Gout suppressant.

Dose : Allopurinol, 200 to 400 mg daily in divided doses.

Usual strength : 100 mg.

Standards : Allopurinol tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Allopurinol, $C_5H_4N_4O$.

Identification : (A) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of the solution obtained in the **Assay** exhibits a maximum only at 250 nm, Appendix 5.15A.

(B) Shake a quantity of the powdered tablets equivalent to 0.1 g of Allopurinol with 5 ml of *dilute sodium hydroxide solution* and add 3 ml of *lithium and sodium molybdophosphotungstate solution* and 5 ml of a 20 per cent w/v solution of *sodium carbonate*; a grey-blue colour is produced.

Disintegration : Maximum time, 30 minutes, Appendix 5.6.1.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.1 g of Allopurinol and shake with 20 ml of *0.05N sodium hydroxide* for fifteen minutes, add sufficient *0.1N hydrochloric acid* to produce 100.0 ml and filter; dilute 10.0 ml of the filtrate to 100.0 ml with *0.1N hydrochloric acid* and dilute 10.0 ml of this solution to 100.0 ml with *0.1N hydrochloric acid.* Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 250 nm, Appendix 5.15A, using *0.1N hydrochloric acid* as blank. Calculate the content of $C_5H_4N_4O$, taking 563 as the value of E(1 per cent, 1-cm) at the maximum at about 250 nm.

Storage : Store in well-closed containers.

Aluminium Hydroxide Gel

Category : Antacid.

Dose : 7.5 to 15 ml.

Description : White, viscous suspension, translucent in thin layers; small amounts of clear liquid may separate on standing.

Standards : Aluminium Hydroxide Gel is an aqueous suspension of hydrated aluminium oxide together with varying quantities of basic aluminium carbonate and bicarbonate. It contains not less than 3.5 per cent w/w and not more than 4.4 per cent w/w of Al_2O_3. It may contain Glycerin, Sorbitol, Sucrose or Saccharin as sweetening agent, peppermint oil or other suitable flavours. It may also contain suitable antimicrobial agents.

Identification : A solution in *dilute hydrochloric acid* gives the reactions of *aluminium*, Appendix 3.1.

pH : Between 5.5 and 8.0, Appendix 5.10.

Ammonium salts : To 25 g in an ammonia distillation apparatus add 25 ml of *sodium hydroxide solution* and 250 ml of *water*, distil about 100 ml, collecting the distillate in 25 ml of *0.1N hydrochloric acid.* Titrate the excess of acid with *0.1N sodium hydroxide*, using *methyl red solution* as indicator; not less than 20 ml of *0.1 N sodium hydroxide* is required.

Arsenic : Not more than 1 part per million, Appendix 3.2.1.

Heavy metals : Not more than 10 parts per million, determined by Method A on a solution prepared by dissolving 5 g in 10 ml of *dilute hydrochloric acid*, filtering if necessary, and diluting to 25 ml with *water*, Appendix 3.2.4.

Chloride : Dissolve 0.5 g in 5 ml of *dilute nitric acid*, boil, cool, dilute to 100 ml with *water* and filter; 25 ml of the filtrate complies with the *limit test for chlorides*, Appendix 3.2.2.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Sulphate : Dissolve 2.5 g in 5 ml of *dilute hydrochloric acid* with the aid of heat. Cool and dilute to 200 ml with *water*. Mix well and filter if necessary. To 10 ml of the filtrate add 2 ml of *dilute hydrochloric acid*; the solution complies with the *limit test for sulphates*, Appendix 3.2.8.

Neutralising capacity : Disperse 5.0 g in 100 ml of *water*, heat to 37°, add 100.0 ml of *0.1N hydrochloric acid* previously heated to 37°, and stir continuously, maintaining the temperature at 37°; pH of the solution, at 37°, after ten, fifteen, and twenty minutes, is not less than 1.8, 2.3 and 3.0, respectively, and at no time is more than 4.0. Add 10.0 ml of *0.5N hydrochloric acid* previously heated to 37°, stir continuously for one hour, maintaining the temperature at 37°, and titrate the solution with *0.1N sodium hydroxide* to pH 3.5; not more than 50.0 ml of *0.1N sodium hydroxide* is required.

Microbial limits : The total microbial count does not exceed 100 per ml. 1 ml meets the requirements of the tests for the absence of *E. coli* and pseudomonas, Appendix 4.5.

Assay : Weigh accurately about 5 g and dissolve in 3 ml of *hydrochloric acid* by warming on a water-bath; cool to below 20° and dilute to 100.0 ml with *water*. To 20.0 ml of this solution, add 40 ml of *0.05M disodium ethylenediaminetetraacetate*, 80 ml of *water*, and 0.15 ml of *methyl red solution*, and neutralise by the dropwise addition of *N sodium hydroxide*. Warm on a water-bath for thirty minutes, add 3 g of *hexamine*, and titrate with *0.05M lead nitrate*, using 0.5 ml of *xylenol orange solution* as indicator. Each ml of 0.05 *M disodium ethylenediaminetetraacetate* is equivalent to 0.002549 g of Al_2O_3.

Storage : Store in tightly-closed containers in a cool place and avoid freezing.

Dried Aluminium Hydroxide Gel

Category : Antacid.

Dose : 0.5 to 1 g.

Description : White, light, amorphous powder containing some aggregates; odourless; tasteless.

Solubility : Insoluble in *water* and in *alcohol*; soluble in dilute mineral acids and in an excess of caustic alkali solutions.

Standards : Dried Aluminium Hydroxide Gel consists largely of hydrated aluminium oxide and varying small quantities of basic aluminium carbonate and bicarbonate. It contains not less than 47.0 per cent of Al_2O_3.

Identification : A Solution in *dilute hydrochloric acid* gives the reactions of *aluminium*, Appendix 3.1.

pH : Not more than 10.0, determined in a 4.0 per cent w/v suspension in *carbon dioxide-free water*, Appendix 5.10.

Ammonium salts : Carry out the test described under Aluminium Hydroxide Gel, using 5.0 g; not less than 22.5 ml of *0.1N sodium hydroxide* is required.

Arsenic : Not more than 5 parts per million, Appendix 3.2.1

Heavy metals : Not more than 60 parts per million, determined by Method A on a solution prepared by dissolving 0.33 g in 10 ml of *dilute hydrochloric acid* with the aid of heat, filtering if necessary, and diluting to 25 ml with *water*, Appendix 3.2.4.

Chloride : Dissolve 0.1 g in 10 ml of *dilute nitric acid*, boil, cool, dilute to 100 ml with *water*, and filter; 25 ml of the filtrate complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphate : Dissolve 0.5 g in 5 ml of *dilute hydrochloric acid*, boil, cool, dilute to 200 ml with *water*, and filter; 25 ml of the filtrate complies with the *limit test for sulphates*, Appendix 3.2.8.

Neutralising capacity : Pass a sufficient quantity, triturated if necessary, through a *sieve* of nominal mesh aperture 150 μm. Weigh accurately 0.5 g of the sifted material and add to 200.0 ml of *0.05N hydrochloric acid* previously heated to 37° and complete the test for **Neutralising capacity** described under Aluminium Hydroxide Gel, beginning at the words "and stir continuously.....". Not more than 35.0 ml of *0.1N sodium hydroxide* is required.

Microbial limits : 1 g meets the requirements of the test for the absence of *E. coli* and pseudomonas, Appendix 4.5.

Assay : Weigh accurately about 0.4 g and dissolve in a mixture of 3 ml of *hydrochloric acid* and 3 ml of *water* by warming on a water-bath, and complete the **Assay** described under Aluminium Hydroxide Gel, beginning at the words "cool to below 20°....".

Storage : Store in tightly-closed containers.

Aluminium Hydroxide Tablets

Category : Antacid.

Dose : Dried Aluminium Hydroxide Gel, 0.5 to 1.0 g. Aluminium Hydroxide Tablets should be masticated before being swallowed.

Usual strength : 0.5 g.

Standards : Aluminium Hydroxide Tablets con-

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

tain a quantity of aluminium oxide Al_2O_3 equivalent to not less than 45.0 per cent of the stated amount of Dried Aluminium Hydroxide Gel. The tablets may contain a flavouring agent.

Identification : Warm a quantity of the powdered tablets equivalent to about 0.5 g of Dried Aluminium Hydroxide Gel with 10 ml of *dilute hydrochloric acid.* Cool and filter; the filtrate gives the reactions of *aluminium*, Appendix 3.1.

Neutralising capacity : Pass a sufficient quantity of the powder prepared for use in the **Assay** through a *sieve* of nominal mesh aperture 150 µm. Mix 1.0 g with a small quantity of *water* to give a smooth paste and slowly add further quantities of *water* to a total volume of 100 ml. Warm to 37°, add 100.0 ml of *0.1N hydrochloric acid*, previously heated to 37°, and complete the test for **Neutralising capacity** described under Aluminium Hydroxide Gel, beginning at the words "and stir continuously.....". The volume of *0.1N hydrochloric acid* consumed is not less than 230 ml for each g of Dried Aluminium Hydroxide Gel.

Disintegration : The requirement for disintegration does not apply to Aluminium Hydroxide Tablets.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets, avoiding frictional heat. Weigh accurately a quantity of the powder equivalent to about 0.4 g of Dried Aluminium Hydroxide Gel and dissolve as completely as possible in a mixture of 3 ml of *hydrochloric acid* and 3 ml of *water* by warming on a water-bath, cool to below 20°, and dilute to 100.0 ml with *water*. To 20.0 ml of this solution, add 40 ml of *0.05M disodium ethylenediaminetetraacetate*, 80 ml of *water*, and 0.15 ml of *methyl red solution*, and neutralise by the dropwise addition of *N sodium hydroxide*. Warm on a water-bath for thirty minutes, add 3 g of *hexamine*, and titrate with *0.05M lead nitrate*, using 0.5 ml of *xylenol orange solution* as indicator. Each ml of *0.05M disodium ethylenediaminetetraacetate* is equivalent to 0.002549 g of Al_2O_3.

Storage : Store in well-closed containers in a cool place.

Labelling : The label on the container states that the tablet should be chewed or masticated before swallowing.

Aluminium Sulphate

$Al_2(SO_4)_3, x\,H_2O$ Mol. Wt. 342.14 (anhydrous)

Category : Pharmaceutical aid (for mineral carrier for adsorbed vaccines).

Description : White, crystalline powder or crystalline mass or shining plates; odourless; taste, sweet becoming mildly astringent.

Solubility : Freely soluble in *water*; practically insoluble in *alcohol.*

Standards : Aluminium sulphate contains not less than 51.0 per cent and not more than 59.0 per cent of $Al_2(SO_4)_3$. It contains a varying amount of water of crystallisation.

Identification : A solution (1 in 20) gives the reactions of *aluminium*, and of *sulphates*, Appendix 3.1.

pH : Between 3.0 to 4.0, determined in a 2.0 per cent w/v solution in *carbon dioxide-free water*, Appendix 5.10.

Clarity and colour of solution : A 5 per cent w/v solution is clear and colourless.

Alkalis and alkaline earths : Boil a solution of 1 g in 100 ml of *water*, add a few drops of *methyl red solution* and then enough *dilute ammonia solution* until the colour of solution just changes to a distinct yellow. Dilute to 150 ml with *water*, bring to boil and filter while hot. Evaporate 75 ml of the filtrate to dryness and ignite to constant weight. The weight of residue does not exceed 2 mg.

Ammonium salts : Heat 1 g with 10 ml of *sodium hydroxide solution* on a water-bath for one minute; the odour of ammonia is not perceptible.

Arsenic : Not more than 3 parts per million, Appendix 3.2.1.

Heavy metals : Not more than 40 parts per million, determined by Method A, on 0.5 g dissolved in 1 ml of *dilute acetic acid* and sufficient *water* to produce 25 ml, Appendix 3.2.4.

Iron : Add 0.3 ml of *potassium ferrocyanide solution* to 20 ml of a 1 in 150 solution; no blue colour is produced immediately.

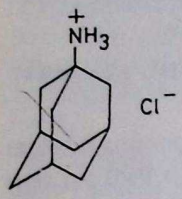
Assay : Weigh accurately about 0.6 g and dissolve in 2 ml of *N hydrochloric acid* and 50 ml of *water*. Add 50.0 ml of *0.05M disodium ethylenediaminetetraacetate* and neutralise to *methyl red solution* with *N sodium hydroxide*. Heat the solution to boiling, leave on a water-bath for 10 minutes, cool rapidly and add about 50 mg of *xylenol orange mixture* and 5 g of *hexamine*. Titrate with *0.05M lead nitrate*. Carry out a blank determination. Each ml of *0.05M disodium ethylenediaminetetraacetate* is equivalent to 0.008554 g of $Al_2(SO_4)_3$.

Storage : Store in well-closed containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Amantadine Hydrochloride



$C_{10}H_{17}N$, HCl Mol. Wt. 187.71

Category : Antiviral (prophylactic).

Dose : 200 mg daily, in a single dose or in two divided doses.

Description : White or nearly white, crystalline powder; odourless; taste, bitter.

Solubility : Freely soluble in *water*; soluble in *alcohol* and in *chloroform*.

Standards : Amantadine Hydrochloride is tricyclo (3.3.1.$1^{3,7}$) dec-1-ylammonium chloride. It contains not less than 98.5 per cent and not more than the equivalent of 101.5 per cent of $C_{10}H_{17}N$, HCl.

Identification : (A) Mix 100 mg with 1 ml of *pyridine* and 0.1 ml of *acetic anhydride* and heat to boiling for about 10 seconds. Pour the hot solution into 10 ml of *dilute hydrochloric acid* and cool to 5°. Collect the precipitate on a sintered-glass filter, wash with *water* and dry "in vacuo at 60°" for one hour; the residue so obtained melts between 147° and 150°.

(B) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

pH : Between 3.0 and 5.5, determined in a 20 per cent w/v solution, Appendix 5.10.

Clarity and colour of solution : Dissolve 2 g in 10 ml of *water*. The solution is clear and nearly colourless.

Heavy metals : Not more than 10 parts per million, determined by Method A, on 2.0 g dissolved in 1 ml of *dilute acetic acid* and sufficient *water* to produce 25 ml, Appendix 3.2.4.

Assay : Weigh accurately about 120 mg, dissolve in 30 ml of *glacial acetic acid*; add 10 ml of *mercuric acetate solution*, and 0.1 ml of *crystal-violet solution*. Titrate with *0.1N perchloric acid* to a blue-green end-point. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.01877 g of $C_{10}H_{17}N$, HCl.

Storage : Store in well-closed containers.

Amantadine Hydrochloride Capsules

Category : Antiviral (prophylactic).

Dose : Amantadine Hydrochloride, 200 mg daily, in a single dose or in two divided doses.

Usual strength : 100 mg.

Standards : Amantadine Hydrochloride Capsules contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Amantadine Hydrochloride $C_{10}H_{17}N$, HCl.

Identification : Place the contents of one capsule in a test-tube, add 2 ml of *pentane* and shake well. Collect the undissolved solid on a sintered-glass filter, wash with two 1-ml portions of *pentane* and dry in air; the residue so obtained complies with **Identification** tests described under Amantadine Hydrochloride.

Other requirements : Comply with the requirements stated under Capsules.

Assay : Weigh accurately a quantity of the mixed contents of 20 capsules equivalent to about 120 mg of Amantadine Hydrochloride and warm in a mixture of 30 ml of *glacial acetic acid* and 10 ml of *mercuric acetate solution*; cool, add 0.1 ml of *crystal violet solution* and titrate with *0.1N perchloric acid* to a blue-green end-point. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.01877 g of $C_{10}H_{17}N$, HCl.

Storage : Store in tightly-closed containers.

Amantadine Hydrochloride Syrup

Category : Antiviral (prophylactic).

Dose : Amantadine Hydrochloride, 200 mg daily, in a single dose or in two divided doses.

Usual strength : 50 mg in 5 ml.

Standards : Amantadine Hydrochloride Syrup contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Amantadine Hydrochloride, $C_{10}H_{17}N$, HCl.

Identification : To 10 ml add 5 ml of *sodium hydroxide solution* and 10 ml of *benzene*. Shake gently for fifteen minutes, remove the benzene layer, dry it over *anhydrous sodium sulphate* and filter. To the filtrate add 1 ml of *pyridine* and 0.1 ml of *acetic anhydride* and evaporate almost to dryness on a water-bath. Dissolve the residue in 5 ml of *dilute hydrochloric acid* by boiling and cool to 5°. Collect the precipitate on a sintered-glass filter, wash with small quantities of *water* and dry "in vacuo at 60°" for

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

one hour. The residue melts between 147° and 150°, Appendix 5.11.

pH : Between 3.5 and 5.0, Appendix 5.10.

Assay : Transfer an accurately measured volume equivalent to 0.2 g of Amantadine Hydrochloride to a separator. Add 5 ml of *sodium hydroxide solution*, 20 ml of *benzene* and shake vigorously for fifteen minutes. Allow the layers to separate and transfer 10.0 ml of the benzene layer to a beaker containing 30 ml of *glacial acetic acid* and three drops of *crystal violet solution*. Titrate with *0.1N perchloric acid* to a blue-green end-point. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.01877 g of $C_{10}H_{17}N,HCl$.

Storage : Store in tightly-closed containers.

Aminocaproic Acid

$NH_2.(CH_2)_5.CO_2H$ Mol. Wt. 131.17

Category : Hemostatic.

Dose : Oral and by intravenous infusion, initial 5 g followed by 1 to 1.25 g every hour to maintain a plasma level of 13 mg per 100 ml. Not more than 30 g per 24-hour period is recommended.

Description : Colourless crystals or white, crystalline powder; odourless; taste, bitter.

Solubility : Freely soluble in *water*, in acids and in alkalis; slightly soluble in *methyl alcohol* and in *alcohol*; practically insoluble in *chloroform* and in *solvent ether*.

Standards : Aminocaproic Acid is 6-aminohexanoic acid. It contains not less than 98.5 per cent of $C_6H_{13}NO_2$, calculated with reference to the dried substance.

Identification : (A) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 100 volumes of *alcohol*, 12 volumes of *water* and 16 volumes of *strong ammonia solution* as the mobile phase. Apply separately to the plate 2 µl of each of two solutions containing (1) 0.25 per cent w/v of the substance being examined and (2) 0.25 per cent w/v of *aminocaproic acid R.S.* After removal of the plate, spray it with a 0.25 per cent w/v solution of *ninhydrin* in a mixture of equal volumes of *methyl alcohol* and *pyridine* and heat at 105° for two minutes. The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

(B) It melts at about 204°, with decomposition, Appendix 5.11.

pH : Between 7.5 and 8.0, determined in a 20 per cent w/v solution, Appendix 5.10.

Colour and clarity of solution : A 20.0 per cent w/v solution is colourless and remains clear for twenty-four hours.

Stability : (1) *Extinction* of a 1-cm layer of a 20.0 per cent w/v solution at 287 nm not greater than 0.10 and at 450 nm, not greater than 0.03, Appendix 5.15A.

(2) Place 20.0 g in an even layer in a shallow dish 9 cm in diameter, cover and allow to stand at 98° to 102° for seventy-two hours. Dissolve in sufficient *water* to produce 100.0 ml and measure the *extinction* of a 1-cm layer of the resulting solution at 287 nm and at 450 nm. *Extinction* at 287 nm, not greater than 0.15 and at 450 nm, not greater than 0.03, Appendix 5.15A.

Heavy metals : Not more than 10 parts per million. determined on 1.0 g, by Method B, Appendix 3.2.4.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.5 g and dissolve in about 100 ml of *glacial acetic acid*, with gentle heat to effect solution, and cool. Add 0.1 ml of *crystal violet solution* and titrate with *0.1N perchloric acid* to blue-green end-point, carry out a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.015120 g of $C_6H_{13}NO_2$.

Storage : Store in tightly-closed containers.

Aminocaproic Acid Injection

Category : Hemostatic.

Dose : Aminocaproic Acid, by slow intravenous infusion, 100 mg per kg of body weight every four to five hours.

Not more than 30 g per 24-hour period is recommended.

Usual strength : 0.4 g per ml.

Standards : Aminocaproic Acid Injection is a sterile solution of Aminocaproic Acid in Water for Injection. It contains not less than 95.0 per cent and not more than 107.5 per cent of the stated amount of $C_6H_{13}NO_2$.

Identification : To a volume equivalent to 0.4 g of Aminocaproic Acid add 2 ml of *solvent ether*, stir, add 2 ml of *methyl alcohol*, stir again, and allow to stand; the crystals after drying comply with **Identification** test (A) described under Aminocaproic Acid.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

pH : Between 6.0 and 7.6, Appendix 5.10.

Pyrogens : Comply with the *test for pyrogens*, Appendix 2.36, using a quantity containing not less than 0.3 g of Aminocaproic Acid per kg of the rabbit's weight, diluted with *water for injection* to produce a solution containing 10 per cent w/v of Aminocaproic Acid.

Other requirements : Complies with the requirements stated under Injections.

Assay : Measure accurately a volume equivalent to 0.5 g of Aminocaproic Acid in a flask, add about 100 ml of *glacial acetic acid*, mix and proceed as directed in the **Assay** under Aminocaproic Acid, beginning at the words "Add 0.1 ml of *crystal-violet solution*....".

Storage : Store in single-dose or multi-dose containers.

Aminocaproic Acid Tablets

Category : Hemostatic.

Dose : Aminocaproic Acid, 5 g followed by 1 to 1.25 g every hour.

Not more than 30 g per 24-hour period is recommended.

Usual strength : 0.5 g.

Standards : Aminocaproic Acid Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Aminocaproic acid, $C_6H_{13}NO_2$.

Identification : Triturate 2 tablets with 10 ml of *water* and filter into 100 ml of *acetone*. Swirl the mixture and allow to stand for fifteen minutes to complete crystallization. Filter through a medium porosity, sintered-glass filter and wash the crystals with 25 ml of *acetone*. Apply vacuum to remove the solvent, then dry at 105° for 30 minutes and cool. The crystals comply with **Identification** test (A) described under Aminocaproic Acid.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 0.5 g of Aminocaproic Acid, add about 100 ml of *glacial acetic acid*, heat gently to effect solution and cool. Proceed as directed in the **Assay** under Aminocaproic Acid, beginning at the words "Add 0.1 ml of *crystal-violet solution*.....".

Storage : Store in tightly-closed containers.

Aminophylline

Theophylline and Ethylenediamine

$C_{16}H_{24}N_{10}O_4$, $x H_2O$ Mol. Wt. 420.43 (anhydrous).

Category : Bronchodilator.

Dose : 0.1 to 0.3 g. By slow intravenous injection, 0.25 to 0.5 g.

Description : White or slightly yellowish granules or powder; odour, slightly ammoniacal; taste, bitter. On exposure to air it gradually loses ethylene-diamine and absorbs carbon dioxide with the liberation of free theophylline.

Solubility : Freely soluble in *water* (the solution usually becomes turbid on standing); practically insoluble in *alcohol* and in *solvent ether*.

Standards : Aminophylline is a stable mixture or combination of theophylline and ethylenediamine with a variable quantity of water. It contains not less than 98.0 per cent and not more than the equivalent of 100.5 per cent of $C_{16}H_{24}N_{10}O_4$, calculated with reference to the anhydrous substance.

Identification : (A) Dissolve about 0.5 g in 25 ml of *water*, add 1 ml of *dilute hydrochloric acid*, with constant stirring, filter, and wash the precipitate with successive small quantities of cold *water*. The precipitate after recrystallisation from hot *water* and drying at 105°, has a melting-range between 270° and 274°, Appendix 5.11.

(B) To 10 mg of the dried precipitate obtained in **Identification** test (A) add 1 ml of *hydrochloric acid* in a porcelain dish, add 0.1 g of *potassium chlorate* and evaporate to dryness on a water-bath; invert the dish over a vessel containing a few drops of *dilute ammonia solution*; the residue acquires a purple colour. Add a solution of fixed alkali; the colour is discharged.

(C) Saturate in *water* a portion of the dried precipitate obtained in **Identification** test (A) and add *tannic acid solution*; a precipitate soluble in excess of the reagent is produced.

Heavy metals : Not more than 10 parts per million, determined by Method A, on a solution obtained by dissolving 2.0 g in 25 ml of *water*, Appendix 3.2.4.

Ethylenediamine : Between 13.5 per cent and 15.0 per cent of $C_2H_8N_2$, calculated with reference to the anhydrous substance and determined by the following method: Weigh accurately about 0.5 g and dissolve in 30 ml of *water*. Titrate with *0.1N hydrochloric acid* using *methyl orange solution* as indicator. Each ml of *0.1N hydrochloric acid* is equivalent to 0.003005 g of $C_2H_8N_2$.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Water : Not more than 8.0 per cent w/w, using 25 ml of *dehydrated pyridine* in place of *dehydrated methyl alcohol*, Appendix 3.3.25.

Assay : Weigh accurately about 0.25 g, add 50 ml of *water* and 8 ml of *dilute ammonia solution* and warm gently on a water-bath until complete solution is effected. Add 20.0 ml of *0.1N silver nitrate*, mix, heat to boiling, and boil for fifteen minutes. Cool to between 5° and 10° for twenty minutes, filter under reduced pressure and wash the precipitate with three quantities, each of 10 ml of *water*. Acidify the combined filtrate and washings with *nitric acid*, and add an excess of 3 ml of the acid. Cool, add 2 ml of *ferric ammonium sulphate solution*, and titrate with *0.1N ammonium thiocyanate*. Each ml of *0.1N silver nitrate* is equivalent to 0.02102 g of $C_{16}H_{24}N_{10}O_4$.

Storage : Store in tightly-closed, light-resistant containers and protect from atmospheric carbon dioxide.

Aminophylline Injection

Theophylline and Ethylenediamine Injection

Category : Bronchodilator.

Dose : Aminophylline, by slow intravenous injection, 0.25 to 0.5 g.

Usual strength : 0.25 g in 10 ml.

Standards : Aminophylline is a sterile solution of Aminophylline in Water for Injection or is a sterile solution of Theophylline in Water for Injection prepared with the aid of Ethylenediamine Hydrate. It contains not less than 93.0 per cent and not more than 102.0 per cent of the stated amount of Aminophylline, $C_{16}H_{24}N_{10}O_4,2H_2O$.

Aminophylline may contain an excess of ethylenediamine but no other substance may be added. It contains a quantity of ethylenediamine $C_2H_8N_2$ equivalent to not more than 23.0 per cent of the stated amount of Aminophylline, $C_{16}H_{24}N_{10}O_4$, $2H_2O$.

Identification : Dilute a volume equivalent to about 0.5 g of Aminophylline with *water* to about 25 ml, and add 1 ml of *dilute hydrochloric acid* with constant surring. Filter, wash the precipitate with a small portion of cold *water*, and dry at 105°; the theophylline so obtained has a melting-range between 270° and 274° and responds to **Identification** tests (B) and (C) described under Aminophylline.

pH : Between 9.0 and 9.6, Appendix 5.10.

Other requirements : Complies with the requirements stated under Injections.

Ethylenediamine : To a volume equivalent to about 0.5 g of Aminophylline add sufficient *water* to produce 30 ml. Titrate with *0.1N hydrochloric acid* using *methyl orange solution* as indicator. Each ml of *0.1N hydrochloric acid* is equivalent to 0.003005 g of $C_2H_8N_2$.

Assay : Measure accurately a volume equivalent to 0.25 g of Aminophylline and dilute with *water* to 40 ml. Add 8 ml of *dilute ammonia solution* and complete the **Assay** described under Aminophylline, beginning at the words "Add 20.0 ml of *0.1N silver nitrate*....". Each ml of *0.1N silver nitrate* is equivalent to 0.02282 g of $C_{16}H_{24}N_{10}O_4$, $2H_2O$.

Storage : Store in single-dose containers, from which carbon dioxide has been excluded.

Labelling : The label on the container states (1) the route of injection, (2) Do not use the Injection if crystals have separated

Aminophylline Tablets

Theophylline and Ethylenediamine Tablets

Category : Bronchodilator.

Dose : Aminophylline, 0.1 to 0.3 g.

Usual strength : 0.1 g.

Standards : Aminophylline Tablets contain not less than 93.0 per cent and not more than 107.0 per cent of the stated amount of Aminophylline, $C_{16}H_{24}N_{10}O_4,2H_2O$.

Identification : (A) Shake a quantity of the powdered tablets equivalent to 0.5 g of Aminophylline with 25 ml of *water* and filter. To the filtrate add 1 ml of *dilute hydrochloric acid*; filter and wash the precipitate with cold *water*, the precipitate complies with the **Identification** tests described under Aminophylline.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 2 g of Aminophylline and transfer to a 200-ml graduated flask with the aid of a mixture of 50 ml of *water* and 15 ml of *dilute ammonia solution*, and allow to stand for thirty minutes with frequent shaking, warming to about 50° if necessary. Cool, add *water* to volume and mix. Centrifuge about 50 ml of the mixture, and pipette a volume of the clear supernatant liquid equivalent to about 0.25 g of Aminophylline into a flask, dilute with sufficient *water* to produce 40 ml and add 8 ml of *dilute ammonia solution*.

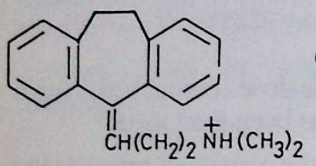
CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Complete the **Assay** described under Aminophylline, beginning at the words "Add 20.0 ml of *0.1N silver nitrate*.....". Each ml of *0.1N silver nitrate* is equivalent to 0.02282 g of $C_{16}H_{24}N_{10}O_4, 2H_2O$.

Storage : Store in tightly-closed, light-resistant containers.

Amitriptyline Hydrochloride



$C_{20}H_{23}N$, HCl Mol. Wt. 313.87

Category : Antidepressant.

Dose : 75 to 150 mg daily, in divided doses; maintenance dose, 50 to 100 mg daily, in divided doses.

Description : Colourless crystals or white or almost white powder; almost odourless; taste, bitter and burning followed by a sensation of numbness.

Solubility : Freely soluble in *water*, in *alcohol*, in *chloroform* and in *methyl alcohol*; practically insoluble in *solvent ether*.

Standards : Amitriptyline Hydrochloride is 3-[10, 11-dihydro-*5H*-dibenzo (*a, d*) cyclohept-5-ylidene] propyldimethylammonium chloride. It contains not less than 99.0 per cent and not more than the equivalent of 105.0 per cent of $C_{20}H_{23}N$,HCl, calculated with reference to the dried substance.

Identification : (A) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.0012 per cent w/v solution in *methyl alcohol* exhibits a maximum only at 239 nm; *extinction* at 239 nm, about 0.55, Appendix 5.15A.

(B) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

(C) To about 50 mg dissolved in 3 ml of *water*, add one drop of a 2.5 per cent w/v solution of *quinhydrone* in *methyl alcohol*; no red colour is produced within fifteen minutes (distinction from nortriptyline).

Melting range : Between 195° and 198°, Appendix 5.11.

pH : Between 4.5 and 6.0, determined in a 1.0 per cent w/v solution, Appendix 5.10.

Heavy metals : Not more than 10 parts per million, determined on 2.0 g by Method B, Appendix 3.2.4.

Ketone : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using a suitable silica gel as the coating substance and a mixture of 3 volumes of *carbon tetrachloride* and 7 volumes of *benzene* as the mobile phase, but allowing the solvent front to travel 12 cm beyond the line of application. Apply separately to the plate 5 µl of each of two solutions in *alcohol* containing (1) 2.0 per cent w/v of the substance being examined and (2) 0.001 per cent w/v of *1,2,4,5-dibenzocyclohepta-1,4-dien-3-one R.S.* After removal of the plate allow it to dry in air until the odour of the solvent is no longer detectable, spray with *sulphuric acid* containing 4 per cent v/v of *formaldehyde solution*, and examine immediately under an ultra-violet lamp having a maximum output at about 366 nm. Any spot in the chromatogram obtained with solution (2) other than the principal spot is more intense than any corresponding spot obtained with solution (1).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying "in vacuo at 60°", Appendix 5.8.

Assay : Weigh accurately about 1.0 g and dissolve in 50 ml of *glacial acetic acid*, warming slightly if necessary, to effect solution. Cool, add 10 ml of *mercuric acetate solution*, two drops of *crystal violet solution* and titrate with *0.1N perchloric acid* to a green end-point. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.03139 g of $C_{20}H_{23}N$, HCl.

Storage : Store in well-closed containers.

Amitriptyline Tablets

Category : Antidepressant.

Dose : Amitriptyline Hydrochloride. 50 to 150 mg daily, in divided doses, maintenance dose, 50 to 100 mg daily, in divided doses.

Usual strengths : 10 mg; 25 mg; 50 mg.

Standards : Amitriptyline Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Amitriptyline Hydrochloride, $C_{20}H_{23}N$, HCl. The tablets may be coated.

Identification : (A) Shake a quantity of the powdered tablets equivalent to about 5 mg of Amitriptyline Hydrochloride with 20 ml of *methyl alcohol* and filter. To 1 ml of the filtrate add 1 ml of a 2.5 per cent w/v solution of *sodium bicarbonate*, 1 ml of a 2 per cent w/v solution of *sodium periodate* and 1 ml of a 0.3 per cent w/v solution of *potassium permanganate*, allow to stand for fifteen minutes, acidify with *dilute sulphuric acid* and extract with 10 ml of *iso-octane*. The light absorption, in

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

the range 230 to 350 nm, of a 1-cm layer of the resulting solution exhibits a maximum only at 265 nm, Appendix 5.15A.

(B) Triturate a quantity of the powdered tablets equivalent to 0.1 g of Amitriptyline Hydrochloride with 10 ml of *chloroform*, filter and evaporate the filtrate to a low volume. Add *solvent ether* until a turbidity is produced and allow to stand. The precipitate complies with **Identification** tests (B) and (C) described under Amitriptyline Hydrochloride.

Ketone : Comply with the test described under Amitriptyline Hydrochloride, using as solution (1) a solution prepared in the following manner: Extract a quantity of the powdered tablets equivalent to 20 mg of Amitriptyline Hydrochloride with 5 ml of a mixture of 1 volume of *dilute hydrochloric acid* and 9 volumes of *alcohol*, centrifuge, and use the supernatant liquid.

Uniformity of content (for 10 mg tablets only): Crush one tablet, shake with 20.0 ml of *0.1N hydrochloric acid* for thirty minutes and centrifuge. On 10.0 ml of the clear supernatant liquid complete the **Assay** beginning at the words "add 5 ml of *water* and 1 g of *sodium chloride*....". Calculate the content of $C_{20}H_{23}N$,HCl.

Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 90 per cent and 110 per cent of the average except that for one tablet the content may be between 85 per cent and 115 per cent of the average.

Other requirements : Comply with the requirements stated under Tablets.

Assay : When tablets are film-coated, shake 20 tablets with *water* until completely disintegrated and dilute with *water* to produce a solution containing about 5 mg of Amitriptyline Hydrochloride in 10 ml.

When the tablets are sugar-coated, weigh and powder 20 tablets. Weigh accurately a quantity of powder equivalent to about 0.1 g of Amitriptyline Hydrochloride and shake with 120 ml of *0.1N hydrochloric acid* for thirty minutes and dilute with *0.1N hydrochloric acid* to produce a solution containing 5 mg of Amitriptyline Hydrochloride in 10 ml.

To 10 ml of the solution add 5 ml of *water* and 1 g of *sodium chloride*, shake for three minutes and make alkaline with *sodium hydroxide solution*. Extract with four quantities, each of 20 ml, of *solvent ether* and wash the combined extracts with two quantities, each of 5 ml, of a mixture of equal parts by volume of a saturated solution of *sodium chloride* and *water*. Extract the ether solution with 20 ml of *0.1N hydrochloric acid* and two quantities, each of 5 ml, of *0.1N hydrochloric acid*, combine the extracts, heat on a water-bath for thirty minutes. Cool, and add sufficient *0.1N hydrochloric acid* to produce 50.0 ml. Dilute 10.0 ml to 100.0 ml with *0.1N hydrochloric acid* and measure the *extinction* of a 1-cm layer of the resulting solution at a maximum at about 239 nm, Appendix 5.15A. Calculate the content of $C_{20}H_{23}N$,HCl taking 445 as the value of E(1 per cent, 1-cm) at the maximum at about 239 nm.

Storage : Store in well-closed containers.

Ammonium Chloride

NH_4Cl Mol. Wt. 53. 49

Category : Expectorant; diuretic; systemic acidifier.

Dose : 3 to 6 g daily, in divided doses.

Description : Colourless crystals or white crystalline powder; odourless; taste, saline.

Solubility : Freely soluble in *water*; sparingly soluble in *alcohol*.

Standards : Ammonium Chloride contains not less than 99.5 per cent of NH_4Cl, calculated with reference to the dried substance.

Identification : It gives the reactions of *ammonium salts* and of *chlorides*, Appendix 3.1.

Clarity and colour of solution : A 10.0 per cent w/v solution is clear and colourless.

pH : Between 4.5 and 6.0, determined in a 5.0 per cent w/v solution, Appendix 5.10

Arsenic : Not more than 4 parts per million, Appendix 3.2.1.

Heavy metals : Not more than 10 parts per million, determined by Method A, on 2.0 g dissolved in 25 ml of *water*, Appendix 3.2.4.

Barium : Dissolve 0.5 g in 10 ml of *water* and add 1 ml of *dilute sulphuric acid*; no turbidity is produced within two hours.

Sulphate : 2 g complies with the *limit test for sulphates*, Appendix 3.2.8.

Thiocyanate : Acidify 10 ml of a 10 per cent w/v solution with *hydrochloric acid* and add a few drops of *ferric chloride solution*; no red colour is produced.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.1 g, dissolve in 20 ml of *water* and add a mixture of 5 ml of *formaldehyde solution*, previously neutralised to *dilute phenolphthalein solution* and 20 ml of *water*. After two minutes, titrate slowly with *0.1N sodium hydroxide*, using a further 0.2 ml of *dilute phenolphthalein*

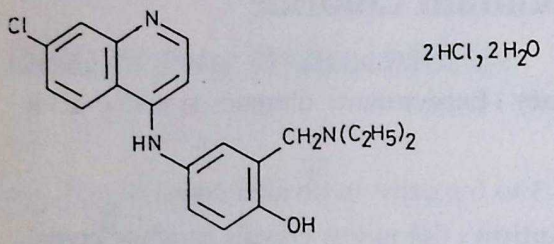
CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

solution. Each ml of *0.1N sodium hydroxide* is equivalent to 0.005349 g of NH_4Cl.

Storage : Store in tightly-closed containers.

Amodiaquine Hydrochloride



$C_{20}H_{22}ClN_3O,2HCl,2H_2O$ Mol. Wt. 464.82

Category : Antimalarial.

Dose : Suppressive, the equivalent of 0.4 g of amodiaquine base weekly. Therapeutic, the equivalent of 0.4 to 0.6 g of amodiaquine base daily for three days.

Description : Yellow, crystalline powder; odourless or almost odourless; taste, bitter.

Solubility : Soluble in *water*; sparingly soluble in *alcohol*; practically insoluble in *chloroform* and in *solvent ether.*

Standards : Amodiaquine Hydrochloride is the dihydrate of the dihydrochloride of 4-(7-chloro-4-quinolylamino)-2-(diethylaminomethyl) phenol.

It contains not less than 97.0 per cent and not more than the equivalent of 103.0 per cent of $C_{20}H_{22}ClN_3O,2HCl$, calculated with reference to the anhydrous substance.

Identification : (A) To 1 ml of a 2 per cent w/v solution, add 0.5 ml of *cobalt thiocyanate solution*, a green precipitate is produced.

(B) The light absorption, in the range 240 to 360 nm, of a 1-cm layer of a 0.0015 per cent w/v solution in *0.1N hydrochloric acid* exhibits a maximum only at 343 nm; *extinction* at 343 nm, about 0.55, Appendix 5.15A.

(C) To 20 ml of a 2 per cent w/v solution, add 1 ml of *dilute ammonia solution.* Shake and filter; the filtrate gives the reactions of *chlorides*, Appendix 3.2.2.

(D) The undried material melts at about 158°, Appendix 5.11.

pH : Between 4.0 and 4.6, determined in a 2.0 per cent w/v solution, Appendix 5.10.

4-(7-Chloro-4-quinolylamino) phenol hydrochloride : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance, spread in a layer about 0.5 mm thick, and a mixture of 5 volumes of *chloroform*, 4 volumes of *ethyl methyl ketone*, and 1 volume of *diethylamine*, as the mobile phase. Apply separately to the plate 5 µl of each of two solutions in *methyl alcohol* containing (1) 10.0 per cent w/v of the substance being examined, and (2) 10.0 per cent w/v of *amodiaquine hydrochloride R.S.* and 0.020 per cent w/v of *4-(7-chloro-4-quinolylamino) phenol hydrochloride R.S.* After removal of the plate, heat it at 105° for ten minutes, spray with a freshly prepared mixture of equal volumes of a 10 per cent w/v solution of *ferric chloride* and a 1 per cent w/v solution of *potassium ferricyanide* and examine immediately. Any spot due to 4-(7-chloro-4-quinolylamino) phenol hydrochloride in the chromatogram obtained with solution (1) is not more intense than the corresponding spot in the chromatogram obtained with solution (2).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7

Water : Between 7 per cent and 9 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately about 0.3 g and dissolve in sufficient *0.1N hydrochloric acid* to produce 200.0 ml. Dilute 10.0 ml to 1000.0 ml with *0.1N hydrochloric acid.* Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 343 nm, Appendix 5.15A, using *0.1N hydrochloric acid* as the blank. Calculate the content of $C_{20}H_{22}ClN_3O$, 2HCl from the *extinction* obtained by carrying out the **Assay** simultaneously on *amodiaquine hydrochloride R.S.* and from the declared content of $C_{20}H_{22}ClN_3O$, 2HCl in the *amodiaquine hydrochloride R.S.*

Storage : Store in tightly-closed containers.

Amodiaquine Tablets

Category : Antimalarial.

Dose : Suppressive, the equivalent of 0.4 g of amodiaquine base weekly. Therapeutic, the equivalent of 0.4 to 0.6 g of amodiaquine base daily for three days.

Usual strength : The equivalent of 0.2 g of amodiaquine base.

Standards : Amodiaquine Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of amodiaquine, $C_{20}H_{22}ClN_3O$.

Identification : (A) Extract the powdered tablets with *water* and filter; the filtrate gives a green precipitate on adding *cobalt thiocyanate solution.*

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

(B) The powdered tablets give the reactions of *chlorides*, Appendix 3.1.

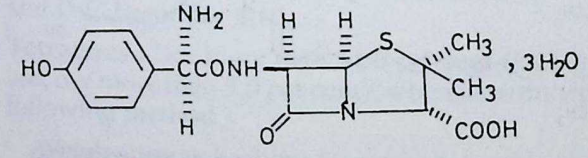
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.3 g of amodiaquine, add 100 ml of *0.1N hydrochloric acid* and heat on a water-bath for about fifteen minutes with occasional stirring. Cool, transfer to a 200-ml graduated flask and dilute to volume with *0.1N hydrochloric acid*. Pipette 10.0 ml of the clear supernatant liquid into a separator, add 10 ml of *0.1N hydrochloric acid* and extract with 20 ml of *chloroform*. Discard the chloroform extract. Add 4.5 ml of *N sodium hydroxide* and extract with four quantities, each of 25 ml, of *chloroform*. Extract the combined chloroform solutions with three quantities, each of 50 ml, of *0.1N hydrochloric acid* and dilute with sufficient *0.1N hydrochloric acid* to produce 200.0 ml. Dilute 10.0 ml with sufficient *0.1N hydrochloric acid* to produce 100.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 343 nm, Appendix 5.15A using *0.1N hydrochloric acid* as the blank. Calculate the content of $C_{20}H_{22}ClN_3O$, 2HCl from the *extinction* obtained by carrying out the **Assay** simultaneously on *amodiaquine hydrochloride R.S.* and from the declared content of $C_{20}H_{22}ClN_3O$, 2HCl in the *amodiaquine hydrochloride R.S.* Multiply the result by 0.830 to give the equivalent quantity of $C_{20}H_{22}ClN_3O$.

Storage : Store in tightly-closed containers.

Labelling : The label on the container states the strength in terms of the equivalent amount of amodiaquine base.

Amoxycillin Trihydrate



$C_{16}H_{19}N_3O_5S,3H_2O$ Mol. Wt. 419.45

Category : Antibacterial.

Dose : The equivalent of 0.75 to 4.5 g of amoxycillin daily, in divided doses.

Description : White, or almost white, crystalline powder.

Solubility : Slightly soluble in *water*, in *alcohol* and in *methyl alcohol*; practically insoluble in *chloroform*, in *solvent ether* and in fixed oils.

Standards : Amoxycillin Trihydrate is the trihydrate of (6*R*)-6-(*α*-*p*-hydroxyphenyl-D-glycylamino) penicillanic acid. It contains not less than 92.0 per cent of $C_{16}H_{19}N_3O_5S$, calculated with reference to the anhydrous substance.

Identification : (A) Suspend 10 mg in 1 ml of *water*, add 2 ml of a mixture of 2 ml of *potassium cupri-tartrate solution* and 6 ml of *water*; a magenta colour is immediately produced.

(B) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silanised silica gel HF 254* as the coating substance and a mixture of 4 volumes of *buffer solution pH 6.0*, and 1 volume of *acetone* as the mobile phase. Apply separately to the plate 1 µl of each of the following two solutions in *buffer solution pH 7.0* containing (1) 0.25 per cent w/v of the substance being examined and (2) 0.25 per cent w/v of *amoxycillin trihydrate R.S.* After removal of the plate, allow it to dry in air, spray with *0.125N sodium hydroxide*, allow to dry in air, spray with a mixture of 100 volumes of *starch solution*, 6 volumes of *glacial acetic acid* and 2 volumes of a 1 per cent w/v solution of *iodine* in a 4 per cent w/v solution of *potassium iodide*. The principal spot in the chromatogram obtained with solution (1) corresponds with the principal spot in the chromatogram obtained with solution (2).

(C) Dissolve 0.1 ml of *aniline* in a mixture of 1 ml of *hydrochloric acid* and 3 ml of *water*. Cool the solution in ice and add 1 ml of a freshly prepared 20 per cent w/v solution of *sodium nitrite*. Add the resulting mixture dropwise to a cold solution of 100 mg of the substance being examined in 2 ml of *5N sodium hydroxide*; the solution becomes deep cherry-red and a dark brown precipitate is produced.

Specific optical rotation : Between +290° and +310° determined in a 0.2 per cent w/v solution, Appendix 5.12.

pH : Between 3.5 and 6.0, determined in a 0.2 per cent w/v solution, Appendix 5.10.

Total amoxycillin; Chloride and Iodine-absorbing substances : Between 95.0 per cent and 103.0 per cent, determined by adding together the percentages of amoxycillin ($C_{16}H_{19}N_3O_5S$), chloride (calculated as NaCl) and iodine-absorbing substances (all calculated with reference to the anhydrous substance), found by the methods described below:

Chloride : Not more than 1.5 per cent, calculated as NaCl with reference to the anhydrous substance. Weigh accurately about 0.3 g, dissolve in 10 ml of *water*, add 10 ml of *nitric acid* and 10.0 ml of *0.1N silver nitrate*; heat for thirty minutes in a water-bath, cool, add 50 ml of *water*, and 2 ml of *nitrobenzene* and titrate with *0.1N ammonium thiocyanate*, using a freshly prepared *ferric ammonium sulphate solution* as indicator. Each ml of *0.1N silver nitrate* is equivalent to 0.005845 g of NaCl.

Iodine-absorbing substances : Not more than 5.0 per cent, calculated with reference to the anhydrous

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

substance. Weigh accurately about 0.1 g and dissolve in *mixed phosphate buffer pH 7.0* to produce 100.0 ml. To 5.0 ml add 5 ml of *mixed phosphate buffer pH 4.0* and 5 ml of *0.02N iodine*, close the flask with a moistened stopper and allow to stand in the dark for ten minutes. Titrate with *0.01N sodium thiosulphate* using *starch solution*, added towards the end of the titration, as indicator. To a further 5 ml of *mixed phosphate buffer pH 4.0* add 5 ml of *0.02N iodine* and complete the operation described above, beginning at the words "close the flask.....". The difference between the titrations represents the amount of iodine-absorbing substances present. Each ml of *0.01N sodium thiosulphate* is equivalent to 0.000372 g of iodine-absorbing substances.

Water : Between 11.5 per cent and 14.0 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately about 0.17 g and dissolve in sufficient *water* to produce 500.0 ml. Transfer 10.0 ml of the resulting solution to a 100-ml graduated flask, add 10 ml of *buffer solution pH 9.0* followed by 1 ml of *acetic anhydride-dioxan solution*, allow to stand for five minutes, and add sufficient *water* to produce 100.0 ml. Pipette 2 ml of the resulting solution into each of two stoppered tubes. To one tube add 10 ml of *imidazole-mercury reagent*, mix, stopper the tube and immerse in a water-bath at 60° for exactly twenty-five minutes, with occasional swirling. Remove the tube from the water-bath and cool rapidly to 20° (solution 1). To the second tube add 10 ml of *water* and mix (solution 2). Without delay measure the *extinctions* of solutions (1) and (2) at the maximum at about 325 nm, Appendix 5.15A, using as the blank a mixture of 2 ml of *water* and 10 ml of *imidazole-mercury reagent* for solution (1) and *water* for solution (2). Calculate the content of $C_{16}H_{19}N_3O_5S$ from the difference between the *extinctions* of solution (1) and that of solution (2) and from the difference obtained by repeating the operation using 0.17 g of *amoxycillin trihydrate R.S.* instead of the substance being examined and the declared content of $C_{16}H_{19}N_3O_5S$ in the *amoxycillin trihydrate R.S.*

Storage : Store in tightly-closed containers, in a cool place.

Labelling : The label on the container states (1) the date after which the contents are not intended to be used; (2) the storage conditions.

Amoxycillin Capsules

Category : Antibacterial.

Dose : The equivalent of 0.75 to 4.5 g of amoxycillin daily, in divided doses.

Usual strengths : The equivalent of 0.25 g and 0.5 g of amoxycillin.

Standards : Amoxycillin Capsules contain a quantity of Amoxycillin Trihydrate equivalent to not less than 92.5 per cent and not more than 110.0 per cent of the stated amount of amoxycillin.

Identification : Shake a quantity of the contents of the capsules equivalent to 0.5 g of amoxycillin with 5 ml of *water* for five minutes; filter, wash the residue first with *ethyl alcohol* and then with *solvent ether*, and dry under reduced pressure for one hour. The residue complies with the **Identification** tests described under Amoxycillin Trihydrate.

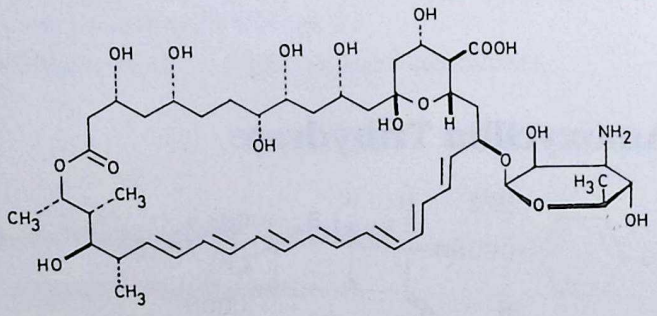
Other requirements : Comply with the requirements stated under Capsules.

Assay : Weigh accurately a quantity of the mixed contents of 20 capsules equivalent to 0.15 g of amoxycillin, add sufficient *water* to produce 500.0 ml, shake for thirty minutes, filter, and complete the **Assay** described under Amoxycillin Trihydrate, beginning at the words "Transfer 10.0 ml.....".

Storage : Store in tightly-closed containers.

Labelling : The label on the container states (1) the quantity of the active ingredients in terms of the equivalent amount of amoxycillin; (2) the date after which the capsules are not intended to be used; (3) the storage conditions.

Amphotericin B



$C_{47}H_{73}NO_{17}$ Mol. Wt. 924.09

Category : Antifungal.

Dose : Oral, upto 200 mg every six hours.

By slow intravenous injection, 250 µg per kg of body weight daily, increased to 1 mg per kg daily or 1.5 mg per kg on alternate days.

Description : Yellow to orange powder; practically odourless.

Solubility : Insoluble in *water*, in *alcohol*, in *solvent ether* and in *benzene*; slightly soluble in

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

dimethylformamide; soluble in *dimethyl sulphoxide*; slightly soluble in *methyl alcohol*.

Standards : Amphotericin B is a mixture consisting mainly of amphotericin B which is (3*R*, 5*R*, 8*R*, 9*R*, 11*S*, 13*R*, 15*S*, 16*R*, 17*S*, 19*R*, 34*S*, 35*R*, 36*R*, 37*S*)-19-(3-amino-3, 6-dideoxy-β-D-mannopyranosyloxy) -16-carboxy-3, 5, 8, 9, 11, 13, 15, 35-octahydroxy-34, 36-dimethyl-13, 17 epoxyoctatriaconta-20, 22, 24, 26, 28, 30, 32-heptaen-37-olide and other antifungal polyenes produced by the growth of certain strains of *Streptomyces nodosus* or by any other means. It has a potency of not less than 750 Units per mg, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *amphotericin B R.S.*, Appendix 5.15B.

(B) Dissolve 25 mg in 5 ml of *dimethyl sulphoxide*, add sufficient *methyl alcohol* to produce 50 ml, and dilute 2 ml to 200 ml with *methyl alcohol*. The light absorption of the resulting solution, in the range 300 to 450 nm, exhibits three maxima, at about 362 nm, 381 nm, and 405 nm. Ratio of the *extinction* at the maximum at about 362 nm, to the *extinction* at the maximum at about 381 nm, about 0.6; ratio of the *extinction* at the maximum at about 381 nm to the *extinction* at the maximum at about 405 nm, about 0.9, Appendix 5.15A.

(C) To 1 ml of a 0.05 per cent w/v solution in *dimethyl sulphoxide* add 5 ml of *phosphoric acid* to form a lower layer; a blue ring is immediately formed at the junction of the liquids; mix, the mixture becomes intensely blue; add 15 ml of *water* and mix; the solution becomes pale straw-coloured.

pH : Between 6.0 and 8.0, determined in a 3.0 per cent w/v suspension in *water*, for parenteral use, between 3.5 and 6.0, Appendix 5.10.

Tetraenes : Not more than 15.0 per cent (for parentera use, not more than 5.0 per cent), when determined by the following method :

Weigh accurately about 50 mg and dissolve in 5 ml of *dimethyl sulphoxide*, add sufficient *methyl alcohol* to produce 50.0 ml, and dilute 4.0 ml to 50.0 ml with *methyl alcohol* (solution 1). Prepare solution (2) in a similar manner using 50 mg of *amphotericin B R.S.* accurately weighed, instead of the substance being examined. For solution (3) dissolve 25 mg of *nystatin R.S.*, accurately weighed, in 25 ml of *dimethyl sulphoxide*, dilute to 250.0 ml with *methyl alcohol* and dilute 4.0 ml to 50.0 ml with *methyl alcohol*. Using as the blank a 0.8 per cent v/v solution of *dimethyl sulphoxide* in *methyl alcohol* measure the *extinctions*, Appendix 5.15 A, of solutions (1) and (2) at the maximum at about 282 nm and that of solution (3) at the same wavelength. Then measure the *extinction* of solution (3) at the maximum at about 304 nm and those of solutions (1) and (2) at the same wavelength. Calculate the E(1 per cent, 1 cm) (specific extinctions) for the substance being examined, *amphotericin B R.S.* and *nystatin R.S.* at both wavelengths and calculate the content of tetraenes from the expression $F+100(B_1S_2-B_2S_1)/(N_2B_1-N_1B_2)$ where S_1 and S_2 are the specific extinctions of the substance being examined at 282 nm and 304 nm respectively, N_1 and N_2 are the specific extinctions of *nystatin R.S.* at 282 nm and 304 nm respectively, B_1 and B_2 are the specific extinctions of *amphotericin B R.S.* at 282 and 304 nm respectively and F is the declared content of tetraenes in *amphotericin B R.S.*

Undue toxicity : Complies with the test described under Cephalexin, Appendix 2.37, using 0.4 ml of a suspension of 0.5 g in 10 ml of a 0.5 per cent w/v solution of *acacia* in *water*.

Sulphated ash : Not more than 3.0 per cent, for parenteral use, not more than 0.5 per cent, Appendix 3.2.7.

Loss on drying : Not more than 5.0 per cent, determined on 1.0 g by drying "in vacuo at 60°", Appendix 5.8.

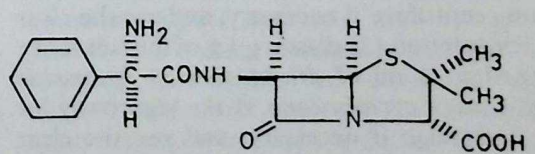
Assay : Weigh accurately about 60 mg, triturate with *dimethylformamide* and add, with shaking, sufficient *dimethylformamide* to produce 100.0 ml. Dilute 10.0 ml to 100.0 ml with *dimethylformamide* and carry out the *microbiological assay of antibiotics, Method A*, Appendix 4.1, and express the results in Units per mg.

Storage : Store in tightly-closed, light-resistant containers in a cold place.

Labelling : The label on the container states (1) the number of Units per mg; (2) whether or not the contents are intended for parenteral administration; (3) the date after which the contents are not intended to be used; (4) the storage conditions.

Ampicillin

Anhydrous Ampicillin



$C_{16}H_{19}N_3O_4S$ Mol. Wt. 349.40

Category : Antibacterial.

Dose : 2 to 6 g daily, in divided doses.

Description : White microcrystalline powder; odourless or almost odourless; taste, bitter.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Solubility : Slightly soluble in *water*, practically insoluble in *alcohol*, in *chloroform*, in *solvent ether*, and in fixed oils.

Standards : Ampicillin is (6*R*)-6-(α-phenyl-D-glycylamino) penicillanic acid. It contains not less than 95.0 per cent of $C_{16}H_{19}N_3O_4S$, calculated with reference to the anhydrous substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *ampicillin R.S.*, Appendix 5.15 B.

(B) Place 0.1 ml of a 0.1 per cent w/v solution of *ninhydrin* on a filter paper, dry at 105°, superimpose 0.1 ml of 0.1 per cent w/v solution of the substance being examined, heat for five minutes at 105°, and allow to cool; a mauve colour is obtained.

(C) Suspend 10 mg in 1 ml of *water*, add 2 ml of a mixture of 2 ml of *potassium cupri-tartrate solution* and 6 ml of *water*; a magenta-violet colour is immediately produced.

Specific optical rotation : Between +280° and +300°, determined in a 0.25 per cent w/v solution, Appendix 5.12.

pH : Between 3.5 and 5.5, determined in a 0.25 per cent w/v solution, Appendix 5.10.

Clarity of solution : Dissolve 1.0 g in 10 ml of *N hydrochloric acid*, and a further 1.0 g in a mixture of 3 ml of *dilute ammonia solution* and 7 ml of *water*. Both solutions are clear or not more than slightly opalescent when freshly prepared.

Dimethylaniline : Carry out the method for gas-liquid chromatography, Appendix 5.4.1, using the following solutions. For solution (1), dissolve 75 mg of *NN-diethylaniline* (internal standard) in a mixture of 2 ml of *hydrochloric acid* and 20 ml of *water*, and add sufficient *water* to produce 50 ml. Dilute 2 ml of the resulting solution to 100 ml with *water* (solution A). Prepare a further solution in exactly the same way as solution A using 50 mg of *dimethylaniline* instead of the 75 mg of internal standard (solution B). To 1 ml of solution B, add 1 ml of solution A, 1 ml of *dilute sodium hydroxide solution* and 1 ml of *cyclohexane*, and shake vigorously for one minute, centrifuge if necessary, and use the clear upper layer. For solution (2) dissolve 1 g of the substance being examined in 3 ml of *dilute sodium hydroxide solution*, add 1 ml of *cyclohexane*, shake vigorously for one minute, centrifuge if necessary, and use the clear upper layer. Solution (3) is prepared in exactly the same way as solution (2) using a mixture of 1 ml of solution A and 2 ml of *dilute sodium hydroxide solution* instead of the 3 ml of *dilute sodium hydroxide solution*.

The chromatographic procedure may be carried out using (a) a glass column 1.5 m long and 0.4 cm in internal diameter packed with 3 per cent w/w of cyanoethylsilicone gum (XE-60 is suitable) on *acid-washed, silanised diatomaceous earth (80 to 100 mesh)* maintained at a temperature of 80°, (b) nitrogen as the carrier gas, and (c) a flame ionisation detector. In the chromatogram obtained with solution (3), the ratio of the area of any peak due to dimethylaniline to the area of the peak due to the internal standard is not greater than the corresponding ratio in the chromatogram obtained with solution (1).

Undue toxicity : Complies with the test described under Bacitracin, Appendix 2.37, using 0.5 ml of a solution containing 20 mg of Ampicillin dissolved in 1 ml of *0.05 N sodium hydroxide*.

Water : Not more than 2.0 per cent w/w, Appendix 3.3.25.

Sulphated ash : Not more than 0.5 per cent, Appendix 3.2.7.

Assay : Weigh accurately about 0.15 g and dissolve in sufficient *water* to produce 500.0 ml. Transfer 10.0 ml of the resulting solution to a 100-ml graduated flask, add 10.0 ml of *buffer solution pH 9.0* followed by 1 ml of *acetic anhydride-dioxan solution*, allow to stand for five minutes, and add sufficient *water* to produce 100.0 ml.

Pipette two 2-ml aliquots of this solution into separate stoppered tubes. To one tube add 10 ml of *imidazole-mercury reagent*, mix, stopper the tube and immerse in a water-bath at 60° for exactly twenty-five minutes, with occasional swirling. Remove the tube from the water-bath and cool rapidly to 20° (solution A). To the second tube add 10 ml of *water* and mix (solution B). Without delay measure the *extinction* of 1-cm layer of solutions A and B at the maximum at about 325 nm, using a mixture of 2 ml of *water* and 10 ml of *imidazole-mercury reagent* for solution A and *water* for solution B as a blank, Appendix 5.15A. Calculate the content of $C_{16}H_{19}N_3O_4S$ from the difference between the *extinction* of solution A and that of solution B and from the difference obtained by repeating the operation using 0.17 g of *ampicillin trihydrate R.S.* instead of the substance being examined and from the declared content of $C_{16}H_{19}N_3O_4S$ in the *ampicillin trihydrate R.S.*

Storage : Store in tightly-closed containers in a cool place.

Labelling : The label on the container states (1) the date after which the contents are not intended to be used; (2) the storage conditions.

Ampicillin Trihydrate

$C_{16}H_{19}N_3O_4S,3H_2O$ Mol. Wt. 403.45

Category : Antibacterial.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Dose : The equivalent of 2 to 6 g of ampicillin daily, in divided doses.

Description : White microcrystalline powder; odourless or almost odourless; taste, bitter.

Solubility : Slightly souble in *water*; practically insoluble in *alcohol*, in *chloroform*, in *solvent ether* and in fixed oils.

Standards : Ampicillin Trihydrate is the trihydrate of (6*R*)-6-(α-phenyl-D-glycylamino) penicillanic acid. It contains not less than 95.0 per cent of $C_{16}H_{19}N_3O_4S$, calculated with reference to the anhydrous substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *ampicillin trihydrate R.S.*, Appendix 5.15 B.

(B) Complies with **Identification** tests (B) and (C) described under Ampicillin.

Specific optical rotation; pH; Clarity of solution; Dimethylaniline; Undue toxicity; Sulphated ash : Complies with the tests described under Ampicillin.

Water : Between 12.0 per cent and 15.0 per cent w/w, Appendix 3.3.25.

Assay : Carry out the **Assay** described under Ampicillin, using 0.17 g.

Storage : Store in well-closed containers, in a cool place.

Labelling : The label on the container states (1) the date after which the contents are not intended to be used; (2) the storage conditions.

Ampicillin Capsules

Category : Antibacterial.

Dose : Ampicillin, 2 to 6 g daily, in divided doses.

Usual strengths : 250 mg; 500 mg.

Standards : Ampicillin Capsules contain a quantity of Ampicillin or Ampicillin Trihydrate equivalent to not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Ampicillin, $C_{16}H_{19}N_3O_4S$.

Identification : (A) The contents of the capsules comply with **Identification** tests (B) and (C) described under Ampicillin.

(B) Shake a quantity of the contents of the capsules equivalent to 0.5 g of Ampicillin with 5 ml of *water* for five minutes, filter, wash the residue first with *alcohol* and then with *solvent ether*, and dry under reduced pressure for one hour. The residue gives the reactions of *penicillins*, Appendix 3.1.

Other requirements : Comply with the requirements stated under Capsules.

Assay : Weigh accurately a quantity of the mixed contents of 20 capsules equivalent to 0.15 g of Ampicillin, add sufficient *water* to produce 500.0 ml, shake for 30 minutes, filter, and complete the **Assay** described under Ampicillin, beginning at the words "Transfer 10.0 ml .....".

Storage : Store in tightly-closed containers in a cool dry place.

Labelling : The label on the container states (1) the strength in terms of the equivalent amount of Ampicillin (when Ampicillin Trihydrate is used); (2) the date after which the contents are not intended to be used; (3) the storage conditions.

Ampicillin for Oral Suspension

Ampicillin Mixture

Category : Antibacterial.

Dose : The equivalent of 1.0 to 2.0 g of Ampicillin daily, in divided doses.

Usual strengths : 125 mg; 250 mg of Ampicillin or the equivalent amount of Ampicillin Trihydrate in 5 ml.

Standards : Ampicillin for Oral Suspension is a mixture of Ampicillin or Ampicillin Trihydrate with one or more suitable colouring, flavouring, sweetening, buffering and suspending agents, preservatives. When reconstituted as directed, it contains not less than 90.0 per cent and not more than 120.0 per cent of the stated amount of Ampicillin, $C_{16}H_{19}N_3O_4S$.

Identification : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *cellulose MN 300* as the coating substance and the aqueous layer obtained after shaking 100 volumes of *0.5M citric acid* with 20 volumes of *butyl alcohol*, as the mobile phase. Apply separately to the plate 2 µl of each of two solutions containing (1) a suitable quantity of the suspension diluted to give a solution containing 0.1 per cent w/v of Ampicillin and (2) 0.1 per cent solution of *ampicillin R.S.* After removal of the plate allow it to dry in air and spray with *starch iodide reagent*. The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

pH : Between 4.5 and 7.0, determined on the suspension obtained by reconstituting as directed on the label of the container, Appendix 5.10.

Water : Not more than 2.5 per cent w/w, Appendix 3.3.25.

Assay : Use either of the following methods; however, the result obtained from the microbiological assay shall be official.

Prepare a suspension as directed on the label of the container, immediately before analysis and reserve a portion for the test for **Stability of suspension.**

(1) Weigh accurately a quantity equivalent to 125 mg of Ampicillin and dilute with sufficient *water* to produce 100.0 ml. On 10.0 ml carry out the **Assay** described under Benzylpenicillin, beginning at the words "Transfer 10.0 ml.....". The difference between the titrations represents the volume of *0.02N iodine* equivalent to the Ampicillin present. Calculate the content of $C_{16}H_{19}N_3O_4S$ from the difference obtained by simultaneously carrying out the assay using *ampicillin trihydrate R.S.* instead of the substance being examined and the declared content of $C_{16}H_{19}N_3O_4S$ in the *ampicillin trihydrate R.S.* Determine the weight per ml of the suspension and calculate the concentration of Ampicillin, weight in volume.

(2) Weigh accurately a quantity equivalent to 100 mg of Ampicillin and dilute with sufficient *buffer solution No. 2*, Appendix 7.1 Table 2, to give a solution containing 0.1 µg of Ampicillin per ml. Carry out the *microbiological assay of antibiotics, Method A*, Appendix 4.1. Determine the weight per ml of the suspension and calculate the concentration of Ampicillin, weight in volume.

Stability of suspension : Store at 22° to 25° for four days the portion of the suspension reserved in the **Assay** and then repeat the **Assay** on the stored suspension. The concentration of Ampicillin in the stored suspension is not less than 90.0 per cent of the concentration found in the freshly prepared mixture.

Storage : Store in well-closed containers in a cool place. The reconstituted suspension should be stored in a cool place and used within four days of preparation.

Labelling : The label on the container states (1) the directions for preparing the suspension; (2) the strength as the equivalent weight of Anhydrous Ampicillin in a suitable dose volume; (3) the period within which the prepared suspension should be used; (4) the date after which the contents are not intended to be used; (5) the storage conditions.

Ampicillin Sodium

$C_{16}H_{18}N_3NaO_4S$ Mol. Wt. 371.39

Category : Antibacterial.

Dose : By intramuscular injection, the equivalent of 1 to 8 g of Ampicillin daily, in divided doses.

Description : White crystalline powder, odourless; taste, bitter; hygroscopic.

Solubility : Freely soluble in *water*; sparingly soluble in *acetone*; slightly soluble in *chloroform*; practically insoluble in *solvent ether*, in *liquid paraffin* and in fixed oils.

Standards : Ampicillin Sodium is sodium 6-[D(−)-2-amino-2-phenylacetamide] penicillanate. It contains not less than 85.0 per cent of $C_{16}H_{19}N_3O_4S$, calculated with reference to the anhydrous substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar intensities to, those in the spectrum of *ampicillin sodium R.S.*, Appendix 5.15B.

(B) Complies with **Identification** tests (B) and (C) described under Ampicillin.

(C) A solution (1 in 20) gives the reactions of *sodium*, Appendix 3.1.

Specific optical rotation : Between +258° and +287° determined in a 0.25 per cent w/v solution in *0.02M potassium hydrogen phthalate*, Appendix 5.12.

pH : Between 7.5 and 10.0, determined in a 10 per cent w/v solution, Appendix 5.10.

Clarity of solution : Dissolve 1.0 g in 10 ml of *water*. The solution is clear or not more than slightly opalescent.

Dimethylaniline : Complies with the test described under Ampicillin.

Dichloromethane : Not more than 0.2 per cent w/w, determined in the following manner: Carry out the method for *gas-liquid chromatography*, Appendix 5.4.1, using solutions in *water* containing (1) 0.02 per cent v/v of *dichloromethane* and 0.02 per cent v/v of *propyl alcohol* (internal standard), (2) 10 per cent w/v of the substance being examined, and (3) 10 per cent w/v of the substance being examined and 0.02 per cent v/v of internal standard.

The chromatographic procedure may be carried out using (a) a glass column 1.5 m long and 0.5 cm in internal diameter packed with 10 per cent w/w of *polyethylene glycol 1500* supported on white diatomaceous earth (100–120 mesh), maintained at 75°, (b) nitrogen as the carrier gas, and (c) a flame-ionisation detector. Calculate the percentage w/w of dichloromethane, assuming the weight per ml, at 20° to be 1.325 g.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Iodine-absorbing substances : Dissolve 0.25 g in sufficient *water* to produce 100 ml. To 10 ml add 0.5 ml of *N hydrochloric acid* and 10 ml of *0.02N iodine* and titrate immediately with *0.02N sodium thiosulphate*, using *starch solution*, added towards the end of the titration, as indicator. Repeat the operation without the substance being examined; the difference between the titrations represents the amount of iodine-absorbing substances present. Each ml of *0.02N sodium thiosulphate* is equivalent to 0.7392 mg of iodine-absorbing substances. Calculate the percentage of iodine-absorbing substances in the substance being examined. The sum of the percentage of iodine-absorbing substances and that of $C_{16}H_{19}N_3O_4S$ as determined by the **Assay**, both calculated with reference to the anhydrous substance, is not less than 92.0 per cent.

Heavy metals : Not more than 20 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

Water : Not more than 2.0 per cent w/w, Appendix 3.3.25.

Assay : Carry out the **Assay** described under Ampicillin, using 0.17 g.

Ampicillin Sodium intended for parenteral administration complies with the following additional requirements :

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using not less than 6 mg per kg of the rabbit's weight, dissolved in not more than 5 ml of *water for injection.*

Sterility : Complies with the *tests for sterility*, Appendix 4.6.

Undue toxicity : Complies with the test described under Bacitracin, the dose being 0.5 ml of solution containing the equivalent of 40 mg of Ampicillin per ml in *water for injection.*

Storage : Store in tightly-closed containers protected from moisture, and in a cool place. If it is intended for parenteral administration, the container should be sterile and sealed so as to exclude micro-organisms.

Labelling : The label on the container states (1) the date after which the contents are not intended to be used; (2) the storage conditions; (3) whether or not the material is intended for parenteral administration.

Ampicillin Injection

Category : Antibacterial.

Dose : By intramuscular injection, the equivalent of 1 to 3 g of Ampicillin daily, in divided doses.

Usual strengths : The equivalent of 100 mg, 250 mg, 500 mg and 1 g of Ampicillin.

Standards : Ampicillin Injection is a sterile solution of Ampicillin Sodium in Water for Injection. It is prepared by dissolving the contents of a sealed container in the requisite amount of Water for Injection immediately before use.

Content of ampicillin, $C_{16}H_{19}N_3O_4S$: Determine the weight of the contents of each of ten containers as described in the test for **Uniformity of weight**, under Injection. From the result of the **Assay** calculate the proportionate amount of Ampicillin, $C_{16}H_{19}N_3O_4S$ in each container. This amount does not deviate from the amount stated on the label by a greater percentage than that shown in Column A of the Table of Deviation, except that in one container the amount may deviate by not more than twice the percentage shown.

Other requirements : Complies with the requirements stated under Injections.

The contents of the sealed container comply with the following requirements:

Description : White, crystalline powder; odourless.

Identification; Specific optical rotation; pH; Clarity of solution; Dimethylaniline; Dichloromethane; Iodine-absorbing substances; Heavy metals; Water; Pyrogens; Sterility and Undue toxicity : Comply with the requirements stated under Ampicillin Sodium.

Assay : Carry out the **Assay** described under Ampicillin, using 0.12 g of the mixed contents of ten containers.

Storage : Store in a cool, dry place. The constituted solution should be used immediately after preparation. It should not be allowed to freeze.

Labelling : The label on the sealed container states (1) the quantity of Ampicillin Sodium contained in it in terms of the equivalent amount of Anhydrous Ampicillin; (2) the date after which the contents are not intended to be used; (3) the storage conditions.

Alpha Amylase

Diastase

Category : Digestive enzyme.

Dose : 0.2 to 0.5 g.

Description : Cream to light brown-coloured powder; almost odourless or with faint characteristic odour; hygroscopic.

Solubility : Sparingly soluble in *water* (except

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

when admixed with an insoluble diluent): insoluble in *alcohol* and in *solvent ether*.

Standards : Alpha-amylase is an amylolytic enzyme or mixture of enzymes obtained from fungi such as *Aspergillus oryzae* or from a non-pathogenic variant of bacteria such as *Bacillus subtilis* and with the specific activity for converting starch into dextrin and maltose. It may contain suitable harmless diluents such as Lactose or Dibasic Calcium Phosphate. It has amylase activity of not less than 800 units which represents the number of grams of dry soluble starch digested by 1.0 g of Alpha-amylase under the conditions of the **Assay.**

Loss on drying : Not more than 5.0 per cent, determined on 1.0 g by drying in an oven at 105° for one hour, Appendix 5.8.

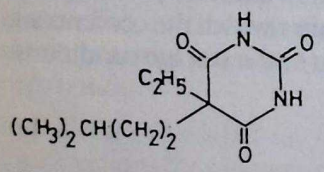
Assay : Carry out the *determination of amylase activity*, Appendix 2.4, and express the result in g of dry soluble starch digested by 1 g.

Storage : Store in tightly-closed containers in a cool dry place.

Labelling : The label on the container states (1) the nature of the enzyme—"fungal" or "bacterial"; (2) the name of the organism from which the enzyme is derived; (3) the amylase activity in terms of units or the weight in grams of starch digested by one gram of the enzyme; (4) the name of any added diluent.

Amylobarbitone

Amobarbital



$C_{11}H_{18}N_2O_3$ Mol. Wt. 226.27

Category : Hypnotic and sedative.

Dose : As a hypnotic, 0.1 to 0.2 g. As a sedative, up to 0.6 g daily, in divided doses.

Description : White crystalline powder; odourless; taste, slightly bitter.

Solubility : Very slightly soluble in *water*; freely soluble in *alcohol* and in *solvent ether*; soluble in *chloroform* and in aqueous solutions of alkali hydroxides and carbonates.

Standards : Amylobarbitone is 5-ethyl-5-isopentylbarbituric acid. It contains not less than 98.5 per cent of $C_{11}H_{18}N_2O_3$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to those in the spectrum of *amylobarbitone R.S.*, Appendix 5.15 B.

(B) Dissolve 50 mg in 2 ml of a 0.2 per cent w/v solution of *cobalt acetate* in *methyl alcohol*, warm, add 50 mg of powdered *borax*, and heat to boiling; a bluish-violet colour is produced.

(C) Triturate 0.6 g with 0.15 g of *anhydrous sodium carbonate* and 5 ml of *water*, add a solution of 0.45 g of *4-nitrobenzyl chloride* in 10 ml of *alcohol* and warm on a water-bath for thirty minutes. Cool, allow to stand for one hour, filter and wash the residue with 10 ml of *N sodium hydroxide* and then with *water*. The residue, after recrystallisation from *alcohol* melts at about 150° or at about 168°, Appendix 5.11.

Melting range : Between 155° and 159°, Appendix 5.11.

Neutral and basic substances : Dissolve 1 g in a mixture of 2 ml of *sodium hydroxide solution* and 13 ml of *water*. Shake with 25 ml of *solvent ether* for one or two minutes. Separate the ethereal layer and wash it thrice, each with 5 ml of *water*. Evaporate the ether and dry the residue at 105° for one hour; the residue weighs not more than 3 mg.

Heavy metals : Not more than 20 parts per million, determined by Method C on 1.0 g dissolved in a mixture of 5 ml of *N sodium hydroxide* and 20 ml of *water*, Appendix 3.2.4.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.5 g and dissolve in 40 ml of *dimethylformamide*, add a few drops of *quinaldine red solution* and titrate with *0.1 N lithium methoxide*, taking care to prevent absorption of atmospheric carbon dioxide. Perform a blank determination and make any necessary correction. Each ml of *0.1 N lithium methoxide* is equivalent to 0.022630 g of $C_{11}H_{18}N_2O_3$.

Storage : Store in well-closed containers.

Amylobarbitone Tablets

Amobarbital Tablets

Category : Hypnotic and sedative.

Dose : Amylobarbitone, as a hypnotic, 0.1 to 0.2 g;

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

as a sedative, up to 0.6 g daily, in divided doses.

Usual strengths : 50 mg and 100 mg.

Standards : Amylobarbitone Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Amylobarbitone, $C_{11}H_{18}N_2O_3$.

Identification : Heat 0.2 g of the residue obtained in the **Assay** on a water-bath with 25 ml of *alcohol (25 per cent)* until dissolved, filter while hot, and allow to cool. The crystals, after washing with a small quantity of *alcohol (25 per cent)*, melt at about 156°, Appendix 5.11, and comply with **Identification** test (B) described under Amylobarbitone.

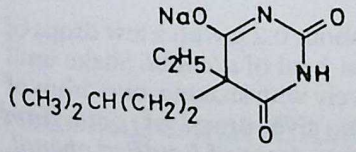
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 50 mg of Amylobarbitone and transfer to a separator with the aid of 15 ml of *water*, add 5 ml of *dilute hydrochloric acid* and extract with four quantities, each of 25 ml of *chloroform*. Filter the combined extracts through a chloroform-washed plug of cotton into a 250 ml graduated flask. Dilute to volume with *chloroform* and mix. Evaporate 5.0 ml of the resulting solution first to dryness and dissolve the residue in 5 ml of *alcohol* and sufficient *buffer solution pH 9.6* to produce 100.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 239 nm, Appendix 5.15 A, using as a blank, a solution prepared by mixing 5 ml of *alcohol* with sufficient *buffer solution pH 9.6* to produce 100.0 ml. Calculate the content of $C_{11}H_{18}N_2O_3$, from the *extinction* obtained by repeating the **Assay** on *amylobarbitone R.S.* and from the declared content of $C_{11}H_{18}N_2O_3$ in the *amylobarbitone R.S.*

Storage : Store in well-closed containers.

Amylobarbitone Sodium

Amobarbital Sodium



$C_{11}H_{17}N_2NaO_3$ Mol. Wt. 248.26

Category : Hypnotic and sedative.

Dose : As a hypnotic, 0.1 to 0.2 g. As a sedative, up to 0.6 g daily, in divided doses.

Description : White, friable, granular powder; odourless; taste, bitter; hygroscopic.

solubility : Very soluble in *water*, soluble in *alcohol*; practically insoluble in *chloroform* and in *solvent ether.*

Standards : Amylobarbitone Sodium is the sodium salt of 5-ethyl-5-isopentylbarbituric acid. It contains not less than 98.5 per cent and not more than the equivalent of 100.5 per cent of $C_{11}H_{17}N_2NaO_3$, calculated with reference to the dried substance.

Identification : Dissolve 1 g in 15 ml of *water*, add 2 ml of *hydrochloric acid*, extract with three quantities, each of 15 ml of *chloroform* and filter. Evaporate the combined filtrates on a water-bath with the aid of a current of air. The residue complies with the following tests:

(A) It melts at about 158°, Appendix 5.11.

(B) It complies with **Identification** tests (B) and (C) described under Amylobarbitone.

pH : Not more than 11.0, determined in a 10.0 per cent w/v solution in *carbon dioxide-free water*, Appendix 5.10.

Neutral and basic substances : Complies with the test for **Neutral and basic substances,** described under Amylobarbitone.

Heavy metals : Not more than 20 parts per million, determined by Method C on 1.0 g dissolved in a mixture of 5 ml of *N sodium hydroxide* and 20 ml of *water*, Appendix 3.2.4.

Free amylobarbitone : Not more than 0.5 per cent, determined by the following method:

Weigh accurately about 1 g, add 50 ml of *benzene* and shake for ten minutes. Filter and repeat the extraction with 25 ml and 10 ml quantities of *benzene*. Combine the filtrates and evaporate to dryness. Dry the residue at 105° for thirty minutes.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105° for four hours, Appendix 5.8.

Assay : Weigh accurately about 0.3 g and dissolve in 5 ml of *ethyl alcohol*. Add 10 ml of *silver nitrate solution* in *pyridine*, five drops of *thymolphthalein solution* and titrate with *0.1N alcoholic sodium hydroxide* to a full blue end-point. Each ml of *0.1N alcoholic sodium hydroxide* is equivalent to 0.02483 g of $C_{11}H_{17}N_2NaO_3$.

Storage : Store in tightly-closed containers, protected from moisture.

Amylobarbitone Sodium Tablets

Amobarbital Sodium Tablets

Category : Hypnotic and sedative.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Dose : Amylobarbitone Sodium, as a hypnotic, 0.1 to 0.2 g; as a sedative, up to 0.6 g daily, in divided doses.

Usual strengths : 50 mg and 100 mg.

Standards : Amylobarbitone Sodium Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Amylobarbitone Sodium, $C_{11}H_{17}N_2NaO_3$.

Identification : (A) Shake a quantity of the powdered tablets equivalent to 0.1 g of Amylobarbitone Sodium with 10 ml of *water* and filter. To the filtrate add 2 ml of *dilute hydrochloric acid*; a white precipitate is produced (distinction from amylobarbitone).

(B) Dissolve 0.2 g of the residue obtained in the **Assay**, in 25 ml of boiling *alcohol (25 per cent)*; filter while hot through a filter paper and allow the filtrate to cool. The crystals melt at about 156°, Appendix 5.11, and comply with **Identification** test (B) described under Amylobarbitone.

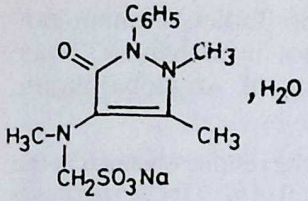
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.2 g of Amylobarbitone Sodium, transfer to a separator and dissolve as completely as possible in 10 ml of a 2 per cent w/v solution of *sodium hydroxide*, saturate with *sodium chloride*, acidify with *hydrochloric acid* and extract with five successive quantities, each of 25 ml of *chloroform*. Filter the combined extracts through a plug of glass wool containing a layer of 2 g of *anhydrous sodium sulphate*. Wash the separator and filter with *chloroform*. Evaporate the solvent in a current of air. Dissolve the residue in a mixture of 5 ml of *water* and 2.5 ml of *strong ammonia solution*; add sufficient *water* to produce 500.0 ml and mix. To 5.0 ml add 0.25 ml of *strong ammonia solution* and sufficient *water* to produce 200.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at a maximum at about 239 nm, Appendix 5.15A. Calculate the content of Amylobarbitone, $C_{11}H_{18}N_2O_3$ from the *extinction* obtained by repeating the **Assay** on *amylobarbitone R.S.* and from the declared content of $C_{11}H_{18}N_2O_3$ in the amylobarbitone R.S. Multiply the result by 1.097 to obtain the content of $C_{11}H_{17}N_2NaO_3$.

Storage : Store in tightly-closed containers.

Analgin

Metamizol



$C_{13}H_{16}N_3NaO_4S, H_2O$ Mol. Wt. 351.40

Category : Analgesic.

Dose : 0.5 to 3 g daily, in divided doses.

Description : White or almost white, crystalline powder with a scarcely perceptible yellowish tinge; odourless; taste, bitter.

Solubility : Freely soluble in *water*; slightly soluble in *alcohol*; practically insoluble in *chloroform* and in *solvent ether*.

Standards : Analgin is the monohydrate of sodium [*N*-(2,3-dihydro-1,5-dimethyl-3-oxo-2-phenyl-1 *H*-pyrazol-4-yl)-*N*-methylamino] methanesulphonate. It contains not less than 99.0 per cent of $C_{13}H_{16}N_3NaO_4S$, calculated with reference to the dried substance.

Identification : (A) Wet about 0.1 g with two drops of *water*; add 5 ml of *alcohol* and 0.5 ml of *dilute hydrochloric acid*. To the solution add 5 ml of *potassium iodate solution*. A crimson colour is produced which deepens on further addition of *potassium iodate solution*.

(B) Heat about 0.2 g with 2 ml of *dilute hydrochloric acid*; the characteristic odour of sulphur dioxide is produced followed by that of formaldehyde.

Acidity or Alkalinity : Dissolve 0.1 g in 10 ml of freshly boiled and cooled *water* and add a few drops of *bromothymol blue solution*; the colour of the solution changes on the addition of not more than 0.05 ml of *0.01N hydrochloric acid* or *0.01N sodium hydroxide*.

Clarity of solution : A 5.0 per cent w/v solution in *water* is clear.

Aminoantipyrine : Wet about 0.2 g with a few drops of *water* in a test-tube and add 3 ml of *alcohol*. Shake until dissolved and add successively with shaking, two drops of *dilute ammonia solution*, five drops of *potassium ferricyanide solution* and two drops of *liquified phenol*, and 5 ml of *water*. The solution acquires a green colour gradually.

Heavy metals : Not more than 20 parts per million, determined by Method A on a solution prepared in the following manner: Ignite 1.0 g until completely ashed. Dissolve the residue in a mixture of 23 ml of *water* and 2 ml of *dilute acetic acid Sp.*, Appendix 3.2.4.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Arsenic : Not more than 1 part per million, Appendix 3.2.1.

Loss on drying : Not more than 5.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.4 g, dissolve in a mixture of 40 ml of *alcohol* and 10 ml of *0.01N hydrochloric acid* and titrate with *0.1N iodine* until a yellow colour which is stable for thirty seconds is produced. Each ml of *0.1N iodine* is equivalent to 0.016670 g of $C_{13}H_{16}N_3NaO_4S$.

Storage : Store in tightly-closed containers.

Analgin Tablets

Metamizol Tablets

Category : Analgesic.

Dose : Analgin, 0.5 to 3 g daily, in divided doses.

Usual strength : 0.5 g.

Standards : Analgin Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Analgin, $C_{13}H_{16}N_3NaO_4S, H_2O$.

Identification : Powder a few tablets and shake a quantity of the powder equivalent to abo t 0.5 g of Analgin with 10 ml of *water* and filter. The filtrate complies with the **Identification** tests described under Analgin.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.5 g of Analgin and transfer to 50-ml volumetric flask. Add 10 ml of *water* and shake for one minute. Dilute to volume with *alcohol*. Shake well and filter. Titrate 25.0 ml of the filtrate with *0.1N iodine* until a yellow colour which is stable for thirty seconds is produced. Each ml of *0.1N iodine* is equivalent to 0.01757 g of $C_{13}H_{16}N_3NaO_4S, H_2O$.

Storage : Store in tightly-closed containers.

Anticoagulant Citrate Dextrose Solution

ACD Solution

Category : Anticoagulant for storage of whole blood.

Usual strengths : *Solution A* – Sodium Citrate 2.2 g, Anhydrous Citric Acid 0.73 g or Citric Acid Monohydrate 0.8 g, Dextrose (Monohydrate) 2.45 g and Water for Injection to 100 ml.

Solution B – Sodium Citrate 1.32 g, Anhydrous Citric Acid 0.44 g or Citric Acid Monohydrate 0.48 g, Dextrose (Monohydrate) 1.47 g and Water for Injection to 100 ml.

NOTE – 15 ml of solution A or 25 ml of solution B are to be used for 100 ml of blood.

Description : Clear, colourless or faintly straw-coloured odourless liquid. Is dextrorotatory.

Standards : Anticoagulant Citrate Dextrose Solution is a sterile solution of Sodium Citrate, Citric Acid, and Dextrose (Monohydrate) in Water for Injection. It contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amounts of Sodium Citrate, $C_6H_5Na_3O_7, 2H_2O$, Citric Acid, $C_6H_8O_7$ and Dextrose, $C_6H_{12}O_6, H_2O$. It contains no antimicrobial agents.

Identification : (A) Complies with **Identification** test (A) described under Dextrose.

(B) It gives the reactions of *sodium*, Appendix 3.1.

(C) It gives the reactions of *citrates*, Appendix 3.1.

pH : Between 4.5 and 5.5, Appendix 5.10.

Chloride : 10 ml complies with the *limit test for chlorides*, Appendix 3.2.2.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36 using per kg of the rabbit's weight, 10 ml of a dilution with *sodium chloride injection* containing 0.5 per cent w/v of Sodium Citrate.

Sterility : Complies with the *tests for sterility*, Appendix 4.6.

Other requirements : Complies with the requirements stated under Injections.

Assay : (1) *For sodium citrate* – Pipette 50 ml into a beaker and titrate with *1.3N hydrochloric acid*, to a pH of 1.98 ± 0.02, determined potentiometrically. Perform a blank determination with 50 ml of *water* and make any necessary correction. Each ml of *1.3N hydrochloric acid* is equivalent to 0.1274 g of $C_6H_5Na_3O_7, 2H_2O$.

(2) *For free citric acid* – Pipette 20 ml into a conical flask and titrate with *0.1N sodium hydroxide* using *phenolphthalein solution* as indicator. Each ml of *0.1N sodium hydroxide* is equivalent to 0.006404 g of $C_6H_8O_7$.

(3) *For dextrose* – Determine the *optical rotation* in a 2-dm tube, Appendix 5.12. The observed rotation multiplied by 1.0425, represents the weight of $C_6H_{12}O_6, H_2O$ in 100 ml of the solution.

Storage : Store in single-dose containers of colourless, transparent glass or of a suitable plastic material.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Labelling : The label on the container states (1) whether the contents are Solution A or Solution B; (2) the number of ml of Solution required per 100 ml of whole blood or the number of ml of Solution required per volume of whole blood to be collected; (3) the date after which the solution is not intended to be used; (4) the storage conditions.

Anticoagulant Citrate Phosphate Dextrose Solution

CPD Solution

Category : Anticoagulant for storage of whole blood.

Usual strength : Sodium Citrate 2.63 g, Citric Acid Monohydrate 0.327 g, Dextrose (Monohydrate) 2.55 g, Sodium Acid Phosphate 0.251 g and Water for Injection to 100 ml.

NOTE—14 ml are to be used for 100 ml of blood.

Description : Clear, colourless, odourless liquid. Is dextrorotatory.

Standards : Anticoagulant Citrate Phosphate Dextrose Solution is a sterile solution of Sodium Citrate, Citric Acid, Sodium Acid Phosphate and Dextrose in Water for Injection. It contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amounts of Sodium Citrate, $C_6H_5Na_3O_7$, $2H_2O$, Citric Acid, $C_6H_8O_7$, H_2O, Sodium Acid Phosphate, NaH_2PO_4, $2H_2O$ and Dextrose $C_6H_{12}O_6$, H_2O. It contains no anti-microbial agents.

Identification : (A) Complies with **Identification** test (A) described under Dextrose.

(B) It gives the reactions of *sodium*, of *citrates*, and of *phosphates*, Appendix 3.1.

pH : Between 5.0 and 6.0, Appendix 5.10.

Chloride : 10 ml complies with the *limit test for chlorides*, Appendix 3.2.2.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using a suitable quantity of the solution diluted with sufficient pyrogen-free *saline solution* to contain 0.5 per cent w/v of Sodium Citrate.

Sterility : Complies with the *tests for sterility*, Appendix 4.6.

Other requirements : Complies with the requirements stated under Injections.

Assay : (1) *For sodium citrate* — Dilute 25.0 ml to 100.0 ml with *water* and mix. Dilute 5.0 ml of the resulting solution to 100.0 ml with *water* and mix. Transfer 1.0 ml of this solution to a test-tube, add 1.3 ml of *pyridine*, swirl to mix, add 5.7 ml of *acetic anhydride*, mix, and immediately place in a water-bath at 30.5° to 31.5°. Allow the colour to develop for thirty-five minutes and then measure the *extinction* of a 1-cm layer of the solution at 425 nm, Appendix 5.15 A, using as the blank solution 1 ml of *water* treated in the same manner. Prepare a calibration curve by measuring the *extinction* of solutions prepared by treating in the same manner 1-ml quantities of suitable dilutions of a solution in *water* containing 2.5 mg per ml of $C_6H_8O_7$, prepared by using *anhydrous citric acid*, previously dried for three hours at 90°. Calculate the total citrate content, as $C_6H_8O_7$, in mg per ml of the solution being examined from the expression 0.2 C, where C is the concentration in µg per ml of $C_6H_8O_7$, read from the curve. Calculate the quantity, in mg of $C_6H_5Na_3O_7$, $2H_2O$ in 1 ml of the solution being examined from the expression 1.53 (A—B), where A is the concentration in mg per ml of total citrate as ($C_6H_8O_7$) and B is the concentration, in mg per ml, of free citric acid in the solution.

(2) *For citric acid* — Carry out the **Assay** for **free citric acid** described under Anticoagulant Citrate Dextrose Solution. From the volume of *0.1N sodium hydroxide* required subtract a volume in ml equal to 1.28 times the number of mg of NaH_2PO_4, $2H_2O$ present, as determined in the **Assay** *for sodium acid phosphate* Each ml of the remainder is equivalent to 0.007005 g of $C_6H_8O_7$, H_2O.

(3) *For sodium acid phosphate* — Dilute 5.0 ml to 100.0 ml with *water*. Transfer 5.0 ml to a 25-ml graduated flask and add 10.0 ml of a 2.8 per cent w/v solution of *sulphuric acid* followed by 2.0 ml of a 2.5 per cent w/v solution of *ammonium molybdate*, mixing after each addition. Add 1.0 ml of *aminohydroxynaphthalein sulphonic acid solution*, and sufficient *water* to produce 25.0 ml; mix and keep aside at 25° for ten minutes. Measure the *extinction* (E_1) at 660 nm, Appendix 5.15A, of a 1-cm layer of the resulting solution using as the blank 5 ml of *water* treated in the same manner. Calculate the content of NaH_2PO_4, $2H_2O$ in each ml of the solution being examined from the *extinction* (E_2) obtained by simultaneously carrying out the operation using 5 ml of a solution of *potassium dihydrogen phosphate* containing 0.11 mg of KH_2PO_4 per ml (C) and from the expression $22.92\ C(E_1/E_2)$.

(4) *For dextrose* — Weigh a clean, medium-porosity sintered-glass crucible containing a few glass beads. To 50 ml of *potassium cupri-tartrate solution* add the glass beads from the weighed crucible, 45 ml of *water* and 5 ml of the solution being examined. Heat the solution at such a rate that it begins to boil in three and a half minutes to four minutes, boil the solution for exactly two minutes, and filter immediately through the weighed crucible, taking care to transfer all the glass beads to the crucible, along with the precipitate. Wash the precipitate with hot *water* and then with 10 ml of *alcohol* and dry it to constant

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

weight at 110°. Perform a blank determination. Each mg of precipitate is equivalent to 0.000496 g of $C_6H_{12}O_6$, H_2O.

Storage : Store in single-dose containers of colourless, transparent glass or of suitable plastic material.

Labelling : The label on the container states (1) the composition and volume of the solution; (2) the date after which the solution is not intended to be used; (3) the storage conditions.

Anticoagulant Sodium Citrate Solution

Category : Anticoagulant for plasma and for blood for fractionation.

Description : Clear, colourless solution.

Standards : Sodium Citrate Anticoagulant Injection is a sterile solution of Sodium Citrate in Water for Injection. It contains not less than 3.8 per cent and not more than 4.2 per cent w/v of $C_6H_5Na_3O_7$, $2H_2O$. It contains no bacteriostatic agents.

Identification : When evaporated to a concentration of 1 in 20 it gives the reactions of *sodium*, and of *citrates*, Appendix 3.1.

pH : Between 6.4 and 7.5, Appendix 5.10.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using a suitable quantity of the solution diluted with sufficient pyrogen-free *saline solution* to contain 0.5 per cent w/v of sodium citrate.

Other requirements : Complies with the requirements stated under Injections.

Assay : Evaporate 10.0 ml to dryness, add 100 ml of *glacial acetic acid*, stir until completely dissolved and titrate with *0.1N perchloric acid*, determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.009803 g of $C_6H_5Na_3O_7$, $2H_2O$.

Storage : Store in single-dose containers of glass or plastic. On keeping, small solid particles may separate from a glass container. A solution containing such particles must not be used.

Antisera

Immunosera

Antisera are native (unconcentrated) sera, or preparations from native sera containing specific immunoglobulins that have a prophylactic or therapeutic action when injected into persons exposed to or suffering from a disease caused by a specific micro-organism.

Antisera are prepared by injecting antigens which are preparations of cultures of the specific organisms or their products into healthy humans or animals such as horses so as to produce in them antibodies which are normally associated with the globulin fraction of serum. Antigens commonly used for this purpose are toxins, toxoids and bacterial and viral vaccines. During the process of immunising, the animals may not be treated with penicillin. The globulins may be obtained from the immune serum by enzyme treatment and fractional precipitation or by other physical or chemical methods.

Antisera issued in liquid form are distributed under aseptic conditions into sterile containers which are then sealed to exclude micro-organisms. A suitable antibacterial substance may be added and is invariably added when the final product is filled in multiple-dose containers. The product may be freeze-dried by a procedure which reduces the water content of the final product to less than 1.0 per cent w/w.

Antitoxic sera are prepared from toxins or toxoids—Toxins are obtained by growing certain pathogenic bacteria in artificial culture media whereby toxins are excreted into the substrate and are subsequently separated from the organisms by filtration. Toxins can be rendered non-toxic by adding formaldehyde solution and incubating at 37° for a few weeks. Detoxicated filtrates of toxins prepared in this manner are called toxoids or formol toxoids.

Non-lethal amounts of toxin or the corresponding toxoid are injected in gradually increasing doses into animals. Specific antitoxins are formed in the serum and the animals become actively immune. When a satisfactory degree of immunity is produced, larger volumes of blood are withdrawn from the animals and the plasma or serum is processed to produce specific antisera.

Antibacterial sera are prepared by injecting graded doses of suspensions of living or dead

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

bacteria or preparations from these suspensions into horses or other animals. Antibodies develop in the animals and combine with the antigens of the organisms rendering them susceptible to phagocytosis or lysis. When the blood contains a sufficient amount of antibody it is collected and processed.

Antiviral sera with the exception of Rabies Antiserum are usually obtained from the plasma or serum of human patients who have recovered from virus diseases, of adults who have had any specific disease in the past, or of persons who have been artificially immunised.

Rabies antiserum is obtained from animals by injecting gradually increasing doses of a rabies vaccine, a killed vaccine being used first and when some immunity is established, living virus being used as an antigen. When a sufficient virus-neutralising titre is reached the blood is collected and processed.

Antisera are almost colourless or very faintly yellow liquids free from turbidity. Freeze-dried antisera consists of white or pale yellow powders or friable masses which dissolve in *water* to form colourless or pale yellow liquids having the same characteristics as the corresponding liquid preparations.

Storage of antisera : Antisera should be protected from light and stored at a temperature between 2° and 8°; they should not be allowed to freeze.

General tests : The following requirements refer to liquid antisera and to the reconstituted freeze-dried preparations.

pH : Between 6.0 and 7.0, Appendix 5.10.

Total protein : Not more than 17.0 per cent w/v, by carrying out the *determination of nitrogen, Method C*, Appendix 3.3.5, and multiplying the result by 6.25.

Foreign proteins : When examined by precipitation reactions with specific antisera, they are shown to consist exclusively of protein of the declared animal species.

Phenol (if present) : Not more than 0.25 per cent w/v, Appendix 3.3.9.

Sterility : Comply with the *tests for sterility*, Appendix 4.6.

Undue toxicity : Comply with the *test for undue toxicity for vaccines and sera*, Appendix 2.37.

NOTE—The statements given in this general monograph are intended to be read in conjunction with the monographs on the individual antiserum in the Pharmacopoeia, which refer to preparations for human use; they do not necessarily apply to the corresponding preparations for use in veterinary medicine.

Arachis Oil

Groundnut Oil

Category : Pharmaceutical aid (oleaginous vehicle).

Description : Very pale yellow oily liquid; odour, faint and nut-like; taste, bland.

Solubility : Very slightly soluble in *alcohol* Miscible with *solvent ether*. with *chloroform* and with *light petroleum* (*boiling range, 40° to 60°*).

Standards : Arachis Oil is the refined fixed oil obtained from the seed kernels of one or more of the cultivated varieties of *Arachis hypogaea* Linn. (Fam. Leguminosae).

Identification : Boil 1 g in a flask under a reflux condenser for five minutes with 5 ml of *1.5N alcoholic potassium hydroxide*; add 1.5 ml of *6N acetic acid* and 50 ml of *alcohol* (*70 per cent*), warm until the solution is clear, and cool slowly, with a thermometer in the liquid; the temperature at which the solution becomes turbid is not lower than 36°.

Wt. per ml : Between 0.908 and 0.920 g, Appendix 5.19.

Refractive index : Between 1.467 and 1.470, Appendix 5.14.

Acid value : Not more than 0.5, Appendix 3.3.15.

Iodine value : Between 85 and 105, Appendix 3.3.18.

Saponification value : Between 185 and 196, Appendix 3.3.20.

Rancidity : Shake 1 ml of a 10 per cent v/v solution in *solvent ether* with 1 ml of *hydrochloric acid*, add 1 ml of a 0.1% w/v solution of *phloroglucinol* in *solvent ether*; no red or pink colour develops.

Cottonseed oil : Complies with the test for the *absence of cottonseed oil in other oils*, Appendix 3.3.23.

Sesame oil : Complies with the test for the *absence of sesame oil in other oils*, Appendix 3.3.23.

Unsaponifiable matter : Not more than 1.0 per cent, Appendix 3.3.21.

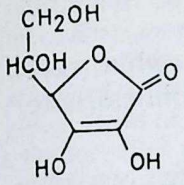
Storage : Store in well-filled, tightly-closed, light-resistant containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Ascorbic Acid

Vitamin C



$C_6H_8O_6$ Mol. Wt. 176.13

Category : Vitamin (antiscorbutic).

Dose : In the prevention of scurvy, 25 to 75 mg daily; in the treatment of scurvy, not less than 250 mg daily, in divided doses.

Description : Colourless crystals or white to very pale yellow crystalline powder; odourless; taste, acid. On exposure to light it gradually darkens.

Solubility : Freely soluble in *water*; sparingly soluble in *alcohol*; insoluble in *chloroform*, in *solvent ether* and in *benzene*.

Standards : Ascorbic Acid is the enolic form of 3-oxo-L-gulofuranolactone. It contains not less than 99.0 per cent and not more than the equivalent of 100.5 per cent of $C_6H_8O_6$.

Identification : (A) Add 2 ml of a 2 per cent w/v solution to a few ml of *2, 6-dichlorophenolindophenol solution*; the solution is decolourised.

(B) Dilute 1 ml of a 2 per cent w/v solution with 5 ml of *water* and add one drop of a freshly prepared 5.0 per cent w/v solution of *sodium nitroprusside* and 2 ml of *dilute sodium hydroxide solution*. Add 0.6 ml of *hydrochloric acid* dropwise and stir. The yellow colour turns blue.

(C) To 2 ml of a 2 per cent w/v solution add 2 ml of *water*, 0.1 g of *sodium bicarbonate* and about 20 mg of *ferrous sulphate*, shake and allow to stand; a deep violet colour is produced; add 5 ml of *dilute sulphuric acid*, the colour disappears.

Specific optical rotation : Between +20.5° and +21.5°, determined in a 10.0 per cent w/v solution, Appendix 5.12.

Light absorption : *Extinction* of a 0.001 per cent w/v solution in *0.01N hydrochloric acid* at the maximum at about 244 nm, about 0.56, Appendix 5.15A.

pH : Between 2.2 and 2.5 determined in a 5.0 per cent w/v solution, Appendix 5.10.

Clarity and colour of solution : Dissolve 1.0 g in sufficient *water* to produce 20.0 ml. The resulting solution is clear and colourless.

Heavy metals : Not more than 20 parts per million, determined by Method A on 1.0 g dissolved in 25 ml of *water*, Appendix 3.2.4.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Assay : Weigh accurately about 0.1 g and dissolve in a mixture of 100 ml of freshly boiled and cooled *water* and 25 ml of *dilute sulphuric acid*. Immediately titrate with *0.1N iodine*, using *starch solution* as indicator as the end-point is neared. Each ml of *0.1N iodine* is equivalent to 0.008806 g of $C_6H_8O_6$.

Storage : Store in tightly-closed, light-resistant containers and avoid contact with metals.

Ascorbic Acid Injection

Vitamin C Injection

Category : Vitamin (antiscorbutic).

Dose : Ascorbic Acid, maintenance – 60 mg once a day; therapeutic – 0.1 to 0.25 g, one or two times a day.

Usual strength : 0.5 g in 2 ml.

Standards : Ascorbic Acid Injection is a sterile solution of Sodium Ascorbate or of Ascorbic Acid prepared with the aid of Sodium Hydroxide, or Sodium Carbonate or Sodium Bicarbonate in Water for Injection. It contains not less than 95.0 per cent and not more than 115 0 per cent of the stated amount of Ascorbic Acid, $C_6H_8O_6$.

Identification : (A) To a volume equivalent to 5 mg of Ascorbic Acid, add 0.5 ml of *0.1N hydrochloric acid*, 3 drops of *sodium nitroprusside solution* and follow immediately with 1 ml of *0.1N sodium hydroxide*; a transient blue colour is produced.

(B) The solution responds to the flame test for *Sodium*, Appendix 3.1.

pH : Between 5.5 and 7.0, Appendix 5.10.

Other requirements : Complies with the requirements stated under Injections.

Assay : Measure accurately a volume equivalent to about 50 mg of Ascorbic Acid and transfer to a 250-ml volumetric flask. Add 20 ml of *metaphosphoric-acetic acids solution*, dilute with *water* to 250 ml and mix. Accurately measure a volume of the dilution equivalent to about 2 mg of Ascorbic Acid into a 50-ml Erlenmeyer flask, add 5 ml of *metaphosphoric-acetic acids solution* and titrate with *standard 2, 6-dichlorophenolindophenol solution*, until the pink colour persists for at least ten seconds, the titration occupying not more than two minutes. Repeat the experiment with a mixture of 5.5 ml of *metaphosphoric-acetic acids solution* and 15 ml of *water*, omitting the ascorbic acid. From the difference calculate the ascorbic acid in each ml of the Injection from

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

the ascorbic acid equivalent of the standard 2,6-dichlorophenolindophenol solution.

Storage : Store in single-dose, light-resistant containers.

Ascorbic Acid Tablets

Vitamin C Tablets

Category : Vitamin (antiscorbutic).

Dose : Ascorbic Acid, in the prevention of scurvy, 25 to 75 mg daily; in the treatment of scurvy, not less than 250 mg daily in divided doses.

Usual strengths : 50 mg, 100 mg and 500 mg.

Standards : Ascorbic Acid Tablets contain not less than 95.0 per cent and not more than 115.0 per cent of the stated amount of Ascorbic Acid, $C_6H_8O_6$.

Identification : Shake a quantity of the powdered tablets with *water* and filter. The filtrate is acid to *litmus solution*, decolourises *2,6-dichlorophenolindophenol solution*, and reduces *silver nitrate solution* immediately in the cold, producing a black precipitate.

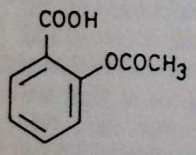
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 0.15 g of Ascorbic Acid and dissolve as completely as possible in a mixture of 30 ml of *water* and 20 ml of *dilute sulphuric acid*. Titrate with *0.1N ceric ammonium sulphate*, using *ferroin sulphate solution* as indicator. Each ml of *0.1N ceric ammonium sulphate* is equivalent to 0.008806 g of $C_6H_8O_6$.

Storage : Store in tightly-closed, light-resistant containers.

Aspirin

Acetylsalicylic Acid



$C_9H_8O_4$ Mol. Wt. 180.16

Category : Analgesic; antipyretic; antirheumatic.

Dose : Analgesic; antipyretic – 0.65 g four to six times a day.

Antirheumatic – 1 g four to six times a day, upto 10 g daily.

Description : Colourless crystals or white crystalline powder; odourless or nearly odourless; taste, slightly acid.

Solubility : Slightly soluble in *water*; freely soluble in *alcohol*; soluble in *chloroform* and in *solvent ether*.

Standards : Aspirin is 2-(acetyloxy) benzoic acid. It contains not less than 99.5 per cent and not more than the equivalent of 100.5 per cent of $C_9H_8O_4$, calculated with reference to the dried substance.

Identification : (A) Boil about 0.5 g with 10 ml of *sodium hydroxide solution* for three minutes, cool and add 10 ml of *dilute sulphuric acid*; a white, crystalline precipitate is produced and the odour of acetic acid is perceptible. Filter, dissolve the precipitate in *water* and to the solution add *ferric chloride test-solution*; a deep violet colour is produced.

(B) Boil about 0.5 g with 10 ml of *N sodium hydroxide* for a few minutes, cool, and add 10 ml of *dilute sulphuric acid*; a white precipitate is formed and the odour of acetic acid is perceptible. Filter, add to the filtrate 3 ml of *alcohol* and 3 ml of *sulphuric acid*, and warm; the odour of ethyl acetate is perceptible.

(C) It melts at about 142°, Appendix 5.11.

Chloride : Boil 2.5 g with 75 ml of *water* for 5 minutes cool, add sufficient *water* to restore the original volume, and filter. A 25 ml portion of the filtrate complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphate : A 25 ml portion of the filtrate prepared for the limit test for **chlorides**, complies with the *limit test for sulphates*, Appendix 3.2.8.

Arsenic ; Not more than 2 parts per million, Appendix 3.2.1.

Heavy metals : Not more than 10 parts per million, determined by the following method: Dissolve 2 g in 25 ml of *acetone*, and add 1 ml of *water* and 10 ml of *hydrogen sulphide solution*; any colour produced is not darker than that of a control made with 25 ml of *acetone*, 2 ml of *standard lead solution* and 10 ml of *hydrogen sulphide solution*.

Readily carbonisable substances : Dissolve 0.50 g in 5 ml of *sulphuric acid* (containing 94.5 per cent to 95.5 per cent w/w of H_2SO_4); the solution is not more coloured than a mixture of 0.2 ml of *cobalt chloride C.S.*, 0.3 ml of *ferric chloride C.S.*, 0.1 ml of *copper sulphate C.S.* and 4.4 ml of *water*.

Salicylic acid : Not more than 0.1 per cent, determined by the following method: Dissolve 2.5 g in sufficient

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

alcohol to produce 25.0 ml (test solution). To each of two matched *Nessler cylinders* add 48 ml of *water* and 1 ml of *a freshly prepared ferric ammonium sulphate reagent* prepared by diluting 1 ml of *N hydrochloric acid* and 2 ml of *ferric ammonium sulphate solution* with sufficient *water* to produce 100 ml. Into one cylinder pipette 1 ml of *standard salicylic acid solution* and into the other pipette 1 ml of the test solution. Mix the contents of the cylinder; after thirty seconds, the colour in the second cylinder is not more intense than that in the cylinder containing the *standard salicylic acid solution*.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent determined on 1.0 g by drying under reduced pressure over *silica gel* for five hours, Appendix 5.8.

Assay : Weigh accurately about 1.5 g, add 50.0 ml of *0.5N sodium hydroxide*, and boil gently for ten minutes. Add *phenol red solution* and titrate the excess of sodium hydroxide with *0.5N sulphuric acid*. Perform a blank determination. Each ml of *0.5N sodium hydroxide* is equivalent to 0.04504 g of $C_9H_8O_4$.

Storage : Store in tightly-closed containers.

Aspirin Tablets

Acetyl Salicylic Acid Tablets

Category : Analgesic; antipyretic; antirheumatic.

Dose : Aspirin, analgesic and antipyretic, 0.6 g four to six times a day; antirheumatic, 1 g four to six times a day, upto 10 g daily.

Usual strengths : 0.15 g, 0.3 g, 0.5 g and 0.6 g.

Standards : Aspirin Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Aspirin, $C_9H_8O_4$.

Identification : Boil 0.5 g of the powdered tablets for two to three minutes with 10 ml of *5N sodium hydroxide*, cool, and add an excess of *N sulphuric acid*; a crystalline precipitate is produced and the odour of acetic acid is perceptible. To a solution of the precipitate in *water*, add *ferric chloride test-solution*; a deep violet colour is produced.

Salicylic acid : Shake a quantity of the powdered tablets equivalent to 0.2 g of Aspirin with 4 ml of *alcohol*, dilute to 100 ml with *water*, filter immediately, transfer 50 ml of the filtrate to a *Nessler cylinder*, add 1 ml of *acid ferric ammonium sulphate solution*, mix, and allow to stand for one minute; the violet colour produced is not deeper than that produced by adding 1 ml of *acid ferric ammonium sulphate solution* to a mixture of 3 ml of a freshly prepared 0.01 per cent w/v solution of *salicylic acid*, 2 ml of *alcohol*, and sufficient *water* to produce 50 ml, contained in a second *Nessler cylinder*.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.5 g of Aspirin, add 30.0 ml of *0.5N sodium hydroxide*, boil gently for ten minutes, and titrate the excess of alkali with *0.5N hydrochloric acid* using *phenol red solution* as indicator. Repeat the operation without the substance being examined; the difference between the titrations represents the amount of *0.5N sodium hydroxide* required by the aspirin. Each ml of *0.5N sodium hydroxide* is equivalent to 0.04504 g of $C_9H_8O_4$.

Storage : Store in tightly-closed containers in a dry place.

Soluble Aspirin Tablets

Soluble Acetylsalicylic Acid Tablets; Dispersion Aspirin Tablets; Calcium Aspirin Tablets

Category : Analgesic; antipyretic; antirheumatic.

Dose : 4 to 12 tablets daily, in divided doses. In the treatment of acute rheumatism, 12 to 24 tablets daily, in divided doses.

Standards : Soluble Aspirin Tablets contain not less than 285 mg and not more than 315 mg of Aspirin, $C_9H_8O_4$ per tablet. Each tablet contains:

Aspirin, in *fine powder*	300 mg
Citric Acid	30 mg
Calcium Carbonate	100 mg
Saccharin Sodium	3 mg

Identification : (A) The tablets effervesce on the addition of *water*.

(B) Boil 0.1 g of the powdered tablets with 10 ml of *water* and add 0.5 ml of *ferric chloride test-solution*; a violet-red colour is produced.

Salicylic acid : To a quantity of the powdered tablets equivalent to 0.5 g of Aspirin, add 25 ml of *chloroform*, shake vigorously for two minutes, and filter through a dry filter paper. Evaporate 5.0 ml of the filtrate rapidly to dryness in a dish in a current of dry air at room temperature. Dissolve the residue in 2 ml of *alcohol*, transfer to a *Nessler cylinder*, using a further 1 ml of *alcohol* to rinse the dish, dilute to 50 ml with *water*, add 1 ml of *acid ferric ammonium sulphate solution*, mix, and allow to stand for one minute; the violet colour produced

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

is not deeper than that produced by adding 1 ml of *acid ferric ammonium sulphate solution* to a mixture of 2 ml of a freshly prepared 0.05 per cent w/v solution of *salicylic acid*, 3 ml of *ethyl alcohol* and sufficient *water* to produce 50 ml, contained in a second *Nessler cylinder*.

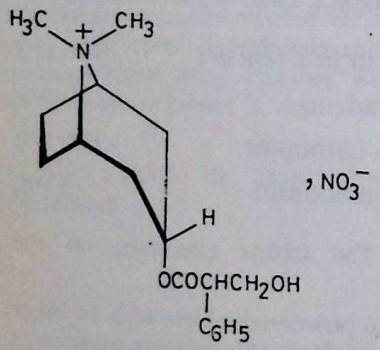
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.3 g of Aspirin with 10 ml of *N sulphuric acid* under a reflux condenser for one hour. Cool, transfer to a separating funnel with the aid of small quantities of *water*, and extract the liberated salicylic acid with four quantities, each of 20 ml, of *solvent ether*. Wash the combined ether extracts with two quantities, each of 5 ml, of *water*, remove the ether in a current of air at a temperature not exceeding 30°, dissolve the residue in 20 ml of *0.5N sodium hydroxide*, and dilute to 200.0 ml with *water*. Transfer 50.0 ml to a stoppered flask, add 50.0 ml of *0.1N bromine* and 5 ml of *hydrochloric acid*, shake repeatedly during fifteen minutes. Add 20 ml of *potassium iodide solution*, shake thoroughly, and titrate with *0.1N sodium thiosulphate*. Each ml of *0.1N bromine* is equivalent to 0.003003 g of $C_9H_8O_4$.

Storage : Store in tightly-closed containers in a dry and cool place.

Atropine Methonitrate

Methylatropine Nitrate



$C_{18}H_{26}N_2O_6$ Mol. Wt. 366.42

Category : Anticholinergic.

Dose : In the treatment of congenital hypertrophic pyloric eteresis of infants: 200 to 600 micrograms, half an hour before feeds.

Description : Colourless crystals, odourless.

Solubility : Freely soluble in *water*; soluble in *alcohol*; practically insoluble in *chloroform* and in *solvent ether*.

Standards : Atropine Methonitrate is (1*R*,3*r*,5*S*)-8-methyl-3-tropoyloxy-tropanium nitrate. It contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of $C_{18}H_{26}N_2O_6$, calculated with reference to the dried substance.

Identification : (A) Add 0.05 ml of a 1 per cent w/v solution to 0.02 ml of a 1 per cent w/v solution of *diphenylamine* in *nitrogen-free sulphuric acid*; an intense blue colour is produced.

(B) To 2.5 ml of 10 per cent solution add 2.5 ml of *water* and 2 ml of *dilute sodium hydroxide solution*; no precipitate is produced.

(C) Add about 1 mg to 4 drops of *fuming nitric acid* and evaporate to dryness on a water-bath. A yellow residue is obtained. To the cooled residue add 2 ml of *acetone* and 4 drops of a 3 per cent w/v solution of *potassium hydroxide* in *methyl alcohol*. A violet colour is produced.

Melting range : Between 166° and 168°, Appendix 5.11.

pH : Between 6.0 and 7.5, determined in a 5.0 per cent w/v solution, Appendix 5.10.

Specific optical rotation : Between −0.25° and +0.05°, determined in a solution containing the equivalent of 10 per cent w/v of the anhydrous salt, in a 2-dm tube, Appendix 5.12.

Silver : To 1 ml of a 10 per cent w/v solution, add 0.2 ml of *sodium sulphide solution*, no darkening in colour is produced.

Halides : To 1 ml of a 10 per cent w/v solution add 0.3 ml of *silver nitrate solution*; no precipitate and not more than a faint opalescence is produced.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

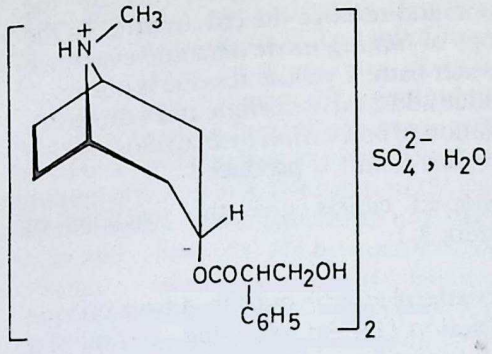
Assay : Weigh accurately about 0.5 g and dissolve in 50 ml of *acetic anhydride*. Titrate with *0.1N perchloric acid*, determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.036640 g of $C_{18}H_{26}N_2O_6$.

Storage : Store in well-closed, light-resistant containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Atropine Sulphate



$C_{34}H_{48}N_2O_{10}S, H_2O$ Mol. Wt. 694.84

Category : Anticholinergic.

Dose : 0.3 to 0.6 mg, three or four times a day. By subcutaneous or intramuscular injection, 0.4 to 0.6 mg.

Description : Colourless crystals, or white, crystalline powder; odourless; taste, very bitter.

Solubility : Very soluble in *water*; freely soluble in *alcohol* and in *glycerin*; slightly soluble in *chloroform*; practically insoluble in *solvent ether*.

Standards : Atropine Sulphate is the monohydrate of (1*R*,3*r*,5*S*)-3-tropoyloxytropanium sulphate. It contains not less than 98.5 per cent and not more than the equivalent of 101.5 per cent of $C_{34}H_{48}N_2O_{10}S$. calculated with reference to the anhydrous substance.

Identification : (A) To a 2 per cent w/v solution, add *sodium hydroxide solution*, filter and transfer the precipitate with *water*. Dry the precipitate at 60° To 5 mg of the residue add five drops of *fuming nitric acid* and evaporate to dryness on a water-bath. Cool the faintly yellow coloured residue and add 2 ml of *acetone* and four drops of a 3 per cent w/v solution of *potassium hydroxide* in *methyl alcohol*. A violet colour is produced.

(B) A solution (1 in 20) gives the reactions of *sulphates*, Appendix 3.1.

Melting range : Not lower than 187°, determined after drying at 120° for four hours, Appendix 5.11.

Optical rotation : Dissolve 3.0 g of the dried substance in sufficient *water* to produce 30.0 ml. The angle of rotation is between −0.50° and +0.05°, Appendix 5.12.

pH : Between 4.5 and 6.2, determined in a 2.0 per cent w/v solution, Appendix 5.10.

Readily oxidisable substances : To 5 ml of a 1.0 per cent w/v solution, add 0.2 ml of *0.1N potassium permanganate*; the colour of the permanganate is not completely discharged within three minutes.

Sulphated ash : Not more than 0.2 per cent, Appendix 3.2.7.

Water : Not more than 4.0 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately about 1.0 g and dissolve in 50 ml of *glacial acetic acid*. Titrate with *0.1N perchloric acid*, determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid*, is equivalent to 0.06770 g of $C_{34}H_{48}N_2O_{10}S$.

Storage : Store in tightly-closed, light-resistant containers.

Atropine Sulphate Injection

Category : Anticholinergic; antidote to cholin esterase inhibitors.

Dose : Atropine Sulphate, Anticholinergic – by subcutaneous, intramuscular, or by intravenous injection, 0.4 to 0.6 mg four to six times a day.

Antidote to cholinesterase inhibitors – by intravenous injection, 2 to 4 mg initially, followed by intramuscular injection, 2 mg repeated every five to ten minutes.

Usual strengths : 0.5 mg per ml; 0.6 mg per ml; 1 mg per ml.

Standards : Atropine Sulphate Injection is a sterile solution of Atropine Sulphate in Water for Injection. The acidity of the solution may be adjusted by the addition of dilute sulphuric acid. It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of $(C_{17}H_{24}NO_3)_2, H_2SO_4, H_2O$.

Identification : Evaporate to dryness a suitable volume. The residue complies with **Identification** test (A) described under Atropine Sulphate.

pH : Between 3.0 and 5.5, Appendix 5.10.

Other requirements : Complies with the requirements stated under Injections.

Assay : Dilute a volume equivalent to 10 mg of Atropine Sulphate to 25 ml with *water* and complete the **Assay** described under Atropine Eye Ointment, beginning at the words "add 75 ml of *chloroform*.....".

Storage : Store in single-dose or multiple-dose containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Atropine Eye Ointment

Category : Mydriatic and cycloplegic.

Usual strength : 1.0 per cent Atropine Sulphate.

Standards : Atropine Eye Ointment is Atropine Sulphate in an eye ointment base. It contains not less than 92.5 per cent and not more than 105.0 per cent of the stated amount of Atropine Sulphate, $(C_{17}H_{23}NO_3)_2, H_2SO_4, H_2O$.

Identification : Dissolve a quantity of the ointment equivalent to 10 mg of Atropine Sulphate as completely as possible in 10 ml of *light petroleum (boiling range, 40° to 60°)* and extract with two quantities, each of 10 ml of *0.1N sulphuric acid*, washing each acid solution with the same 5 ml of *light petroleum (boiling range, 40° to 60°)*. Mix the acid solutions, make alkaline with *dilute ammonia solution*, and extract with two quantities, each of 15 ml of *chloroform*. Remove the chloroform and on the residue, carry out **Identification** test (A) described under Atropine Sulphate.

Other requirements : Complies with the requirements stated under Eye Ointments.

Assay : Weigh accurately a quantity equivalent to 20 mg of Atropine Sulphate, dissolve in 50 ml of *chloroform* and extract with two quantities, each of 10 ml, and one quantity of 5 ml of *water*. To the combined extracts add 75 ml of *chloroform*, 5 ml of *acetate buffer pH 2.8* and 5 ml of *dimethyl yellow-solvent blue 19 solution* and titrate with *dioctyl sodium sulphosuccinate solution* with vigorous swirling, until the colour of the chloroform layer changes from green to pinkish-grey. Repeat the titration on a mixture of 75 ml of *chloroform*, 25 ml of *water* and 5 ml of *acetate buffer pH 2.8* and calculate the content of $(C_{17}H_{23}NO_3)_2, H_2SO_4, H_2O$, from the difference between the titrations and from the result obtained by carrying out the **Assay** on a solution of 20 mg, accurately weighed, of *atropine sulphate* in 25 ml of *water*, beginning at the words "add 75 ml of *chloroform*.....".

Atropine Sulphate Tablets

Category : Anticholinergic.

Dose : Atropine Sulphate, 0.25 to 2 mg daily, in single or divided doses.

Usual strength : 0.5 mg.

Standards : Atropine Sulphate Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Atropine Sulphate, $(C_{17}H_{23}NO_3)_2, H_2SO_4, H_2O$.

Identification : (A) Triturate a quantity of the powdered tablets equivalent to 1 mg of Atropine Sulphate with 1 drop of *strong ammonia solution*, add 2 ml of *chloroform*, and triturate thoroughly, decant the chloroform solution and remove the chloroform. To the residue add 4 drops of *fuming nitric acid* and evaporate to dryness on a water-bath; a yellow residue is obtained. To the cooled residue add 2 ml of *acetone* and 4 drops of a 3 per cent w/v solution of *potassium hydroxide* in *methyl alcohol*; a deep violet colour is produced.

(B) The powdered tablets give the reactions of *sulphates*, Appendix 3.1.

Uniformity of content : Carry out the **Assay** on one tablet using for solution (1), the following: to 5 ml of a 0.004 per cent w/v solution of *atropine sulphate R.S.*, add 1 ml of a 0.02 per cent w/v solution of *homatropine hydrobromide R.S.* (internal standard) in *methyl alcohol* (solution A) and 1 ml of *dilute ammonia solution*. Extract with two quantities, each of 5 ml, of *chloroform*, shake the combined extracts with 1 g of *anhydrous sodium sulphate*, filter and evaporate to dryness. Dissolve the residue in 0.5 ml of a mixture of 20 volumes of *methylene chloride*, 4 volumes of *bis (trimethylsilyl) acetamide* and 1 volume of *trimethylchlorosilane*, mix and allow to stand for thirty minutes. For solution (2) powder one tablet and shake in a centrifuge tube with 5.0 ml of *0.1N hydrochloric acid*; centrifuge, pipette 2.0 ml of the supernatant liquid into a separator and extract with two quantities, each of 2 ml, of *chloroform* and discard the chloroform extracts. Add 1 ml of *dilute ammonia solution* and complete the procedure described under solution (1) beginning at the words "Extract with two quantities, each of 5 ml of *chloroform*.....". For solution (3) pipette 2.0 ml of the supernatant liquid obtained while preparing solution (2), add 1 ml of solution A, extract with two quantities, each of 2 ml, of *chloroform* and discard the chloroform extracts. Add 1 ml of *dilute ammonia solution* and complete the procedure described under solution (1) beginning at the words "Extract with two quantities, each of 5 ml of *chloroform*.....". Calculate the content of $(C_{17}H_{23}NO_3)_2, H_2SO_4, H_2O$ from the declared content of $(C_{17}H_{23}NO_3)_2, H_2SO_4, H_2O$ in *atropine sulphate R.S.*

Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 85 and 115 per cent of the average except that for one tablet the content may be between 80 and 120 per cent of the average.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Carry out the method for *gas-liquid chromatography*, Appendix 5.4.1, using the following solutions: For solution (1) to 10 ml of a 0.05 per cent w/v solution of *atropine sulphate R.S.* add 1 ml of a 0.5 per cent w/v solution of *homatropine hydrobromide R.S.* (internal standard) in *methyl alcohol* (solution A) and 1 ml of *dilute ammonia solution*. Extract with two quanti-

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

ties, each of 10 ml, of *chloroform*, shake the combined extracts with 2 g of *anhydrous sodium sulphate*, filter and evaporate the filtrate to dryness. Dissolve the residue in 2 ml of *methylene chloride*. To 1 ml of this solution, add 0.2 ml of a mixture of 4 volumes of *bis (trimethylsilyl) acetamide* and 1 volume of *trimethylchlorosilane*, mix and allow to stand for thirty minutes. Solution (2) is prepared in a similar manner to solution (3) but omitting the addition of solution A. For solution (3) shake a quantity of the powdered tablets equivalent to 5 mg of Atropine Sulphate with 10 ml of *0.1 N hydrochloric acid*. Add 1 ml of solution A and extract with two quantities, each of 10 ml of *chloroform* and discard the chloroform extracts. Add 1 ml of *dilute ammonia solution* and complete the procedure described under solution (1) beginning at the words "Extract with two quantities, each of 10 ml, of *chloroform*.....". The chromatographic procedure may be carried out using (a) a glass column 1.5 m long and 0.4 cm in internal diameter packed with 3 per cent w/w of phenylmethyl silicone fluid (50 per cent phenyl) on acid-washed, silanised diatomaceous earth (80 to 100 mesh), maintained at 230°, (b) *nitrogen* as the carrier gas and (c) a flame-ionisation detector. Calculate the content of $(C_{17}H_{23}NO_3)_2$, H_2SO_4, H_2O from the declared content of $(C_{17}H_{23}NO_3)_2$, H_2SO_4, H_2O in *atropine sulphate R.S.*

Storage : Store in well-closed containers.

BCG Vaccine (Freeze-dried)

Bacillus Calmette-Guerin Vaccine

Category : Active immunising agent.

Dose : Prophylactic, by intracutaneous injection as a single dose, 0.1 ml.

Standards : BCG Vaccine (Freeze-dried) is a freeze-dried preparation containing live culture of the Bacillus of Calmette and Guerin strain of *Mycobacterium tuberculosis* var. *bovis*.

The vaccine is produced on the basis of the seed lot system. The strain which is of uniform composition is selected and maintained so as to preserve its stability, its power to sensitise man to tuberculin, its ability to protect laboratory animals against tuberculosis and to retain its relative non-pathogenicity for man and laboratory animals. The seed lot is maintained in a freeze-dried form at a temperature not exceeding 6° and is revived by transplanting on to a suitable medium and growing for not more than 7 days. The cultures for harvesting are done on liquid medium and the harvested growth is separated by filtration in the form of a "cake". The "cake" is homogenised in a grinding flask and suspended in a suitable sterile liquid medium designed to preserve the antigenicity and the viability of the vaccine as determined by an appropriate counting method. The suspension is distributed into its final sterile containers and freeze-dried under conditions designed to prevent microbial contamination, particularly by virulent tubercle bacilli. The containers are sealed so as to prevent contamination or deterioration of the final vaccine. The vaccine contains no anti-microbial agent.

Description : White pellet which, when reconstituted, yields an opalescent suspension.

Identification : (A) Examined microscopically in stained smears, the bacilli exhibit the characters of an authentic strain of the Bacillus of Calmette and Guerin.

(B) Colonies grown on a suitable solid culture medium have a characteristic appearance.

Virulent mycobacteria : Reconstitute the vaccine by adding a suitable quantity of the diluent stated on the label, so that it is five times as concentrated as when reconstituted for normal use. Inject 1 ml subcutaneously into each of six healthy guinea-pigs, all of the same sex and weighing between 250 and 300 g and which have not previously been treated with any material which will interfere with the test. The vaccine passes the test if none of the animals dies within 42 days of injection or if only one dies and a post-mortem examination does not reveal, any evidence of tuberculosis infection. If two animals die within this period and a post-mortem examination shows that both are free from tuberculosis, repeat the test on six further guinea-pigs. The vaccine passes the test if none of the second group of animals dies within 42 days of injection or if only one dies and a post-mortem examination reveals no evidence of tuberculosis infection.

Extraneous micro-organisms : Complies with the *tests for sterility*, Appendix 4.6.

Skin-reactivity : Inject intradermally into each of four guinea-pigs, in a volume of 0.1 ml, one, one-tenth and one-hundredth of the human dose of the vaccine and of the *Standard Preparation of BCG Vaccine*. The vaccine passes the test if the skin reactions produced within three weaks do not differ markedly from those produced by the Standard Preparation.

Sterility : Complies with the *tests for sterility*, Appendix 4.6, except that there may be growth of the organism from which the vaccine was prepared.

Toxicity : Inject 0.1 ml intradermally into two guinea-pigs; a definite, non-suppurating nodule but no local necrosis is produced within three weeks of injection.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Potency : (1) *Skin sensitising potency* – Reconstitute the vaccine as for human use with the diluent stated on the label. Inject intradermally 0.1 ml and 0.1 ml of each of a 1 : 10 and a 1 : 100 dilution of the reconstituted vaccine with *saline solution* into each of two or more guinea pigs, each weighing not less than 250 g. Within six weeks of injection, inject intradermally into each guinea-pig 25 Units of Old Tuberculin or Tuberculin Purified Protein Derivative in a volume of 0.1 ml. The vaccine passes the test if the tuberculin induces within twenty-four hours an inflammatory area of induration and oedema not less than 100 mm in diameter.

(2) *For colony-forming units (CFU)* – Carry out the test on at least five containers. Reconstitute the vaccine as for human use with the diluent stated on the label and carry out the *test for colony-forming units (CFU)*, Appendix 4.3.

Storage : Store in hermetically-sealed, light-resistant glass containers at a temperature between 2° and 8°. The reconstituted vaccine should be used immediately after preparation.

Labelling : The label on the container states (1) the name and volume of the liquid to be used for reconstituting the vaccine; (2) the storage conditions; (3) the date after which it is not intended to be used; (4) that any portion of the reconstituted vaccine not used at once should be discarded; (5) that the vaccine should not be exposed to strong daylight before or after reconstitution.

Bacitracin

Category : Antibiotic (for topical use)

Description : White to pale brown powder; odourless or with a faint odour; hygroscopic.

Solubility : Freely soluble in *water*; soluble in *alcohol*, in *methyl alcohol* and in *glacial acetic acid*; practically insoluble in *acetone*, in *chloroform*, and in *solvent ether*.

Standards : Bacitracin is a polypeptide produced by the growth of an organism of the *licheniformis* group of *B. subtilis* (Fam. Bacillaceae). It has a potency of not less than 50 Units of bacitracin activity per mg, calculated with reference to the dried substance.

Identification : Shake 5 mg with 1 ml of *water*, add 1 ml of a 0.2 per cent w/v solution of *ninhydrin* in *n-butyl alcohol* and 0.5 ml of *pyridine*, and heat at 100° for five minutes; a deep purple colour is produced.

pH : Between 5.5 and 7.5, determined in a solution containing 10,000 Units per ml, Appendix 5.10.

Heavy metals : Not more than 30 parts per million, determined on 0.66 g by Method B, Appendix 3.2.4.

Sulphated ash : Not more than 3.0 per cent, Appendix 3.2.7.

Loss on drying : Not more than 5.0 per cent, determined on 0.5 g by drying "in vacuo at 60°" for three hours, Appendix 5.8.

Assay : Carry out the *microbiological assay of antibiotics, Method A*, Appendix 4.1, and express the results in Units per mg.

Bacitracin intended for ophthalmic preparations or for parenteral administration as a spray in body cavities complies with the following additional requirements.

Sterility : Complies with the *tests for sterility*, Appendix 4.6.

Undue toxicity : Inject intravenously into each of five mice, weighing between 18 and 22 g, 0.5 ml of a solution in *saline solution* containing the equivalent of 100 Units of Bacitracin Observe the mice for forty eight hours. None of the mice dies within this period. If one or more animals die within forty-eight hours, repeat the test one or more times using for each test five or more previously unused mice each weighing between 20 and 22 g; the total number of dead animals is not greater than 10 per cent of the total number of animals used, including the original test.

Storage : Store in tightly-closed containers in a cool place. If it is intended for ophthalmic preparations or for parenteral administration the container should be sterile and sealed so as to exclude micro-organisms.

Labelling : The label on the container states (1) the number of Units per mg; (2) the storage conditions; (3) the date after which the contents are not intended to be used.

Bacitracin Zinc

Category : Antibiotic (for topical use).

Description : White or pale buff-coloured powder; odourless or with a faint odour; hygroscopic.

Solubility : Slightly soluble in *water*, and in *alcohol*; very slightly soluble in *solvent ether*; insoluble in *chloroform*.

Standards : Bacitracin Zinc is the zinc salt of Bacitracin. It has a potency of not less than 40 Units of bacitracin activity per mg.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Identification : (A) Complies with the **Identification** test described under Bacitracin.

(B) Ignite the residue gives the reactions of *zinc*, Appendix 3.1.

pH : Between 6.0 and 7.5, determined on the filtrate obtained by shaking 1 g with 10 ml of *carbon dioxide free water*, Appendix 5.10.

Bacitracin F and related substances : Determine the *extinction* of a 1-cm layer of a 0.03 per cent w/v solution in *0.1N sulphuric acid* at 252 nm and 290 nm, Appendix 5.15 A. The ratio of the *extinction* at 290 nm to that at 252 nm is not greater than 0.15.

Zinc content : Between 4.0 per cent and 8.0 per cent, calculated with reference to the dried substance, determined by the following method: Weigh accurately about 0.2 g and dissolve in 20 ml of *water* and 3 ml of *strong ammonia-ammonium chloride solution*; titrate with *0.01M disodium ethylenediamine tetraacetate*, using *mordant black 11 mixture* as the indicator. Each ml of *0.01M disodium ethylenediamine tetraacetate* is equivalent to 0.0006537 g of Zn.

Loss on drying : Not more than 5.0 per cent, determined on 0.5 g by drying "in vacuo at 60°" for three hours, Appendix 5.8.

Assay : Weigh accurately about 0.1 g, suspend in 10 ml of *water* and 0.5 ml of *dilute hydrochloric acid* and add sufficient *water* to produce 200.0 ml. Allow to stand at room temperature for thirty minutes. On the resulting solution carry out the *microbiological assay of antibiotics, Method A*, Appendix 4.1, and express the results in Units per mg

Bacitracin Zinc intended for ophthalmic preparations or for parenteral administration as a spray in body cavities complies with the following additional requirements.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using 1 ml per kg of the rabbit's weight of the supernatant liquid obtained by centrifuging a suspension in *saline solution* containing 600 Units per ml.

Sterility : Complies with the *tests for sterility*, Appendix 4.6.

Undue toxicity : Complies with the test for **Undue toxicity,** described under Bacitracin, using 20 Units suspended in not more than 0.5 ml of *saline solution* and injecting the suspension intraperitoneally; a suitable suspending agent may be used in the preparation.

Storage : Store in tightly-closed containers. If it is intended for ophthalmic preparations or for parenteral administration, the container should be sterile and sealed so as to exclude micro-organisms.

Labelling : The label on the container states (1) the number of Units per mg; (2) the storage conditions; (3) the date after which the contents are not intended to be used.

Barium Sulphate

$BaSO_4$ Mol. Wt. 233.39

Category : Diagnostic aid (radio-opaque medium)

Description : Fine, heavy, white powder free from gritty particles; odourless; tasteless.

Solubility : Practically insoluble in *water*, in organic solvents, and in dilute solutions of acids and alkalies.

Standards : Barium Sulphate contains not less than 97.5 per cent and not more than the equivalent of 100.5 per cent of $BaSO_4$.

Identification : (A) Boil 0.2 g with 5 ml of a 50 per cent w/v solution of *sodium carbonate* for five minutes, add 10 ml of *water*, filter and acidify a part of the filtrate with *dilute hydrochloric acid*. The solution gives the reactions of *sulphates*, Appendix 3.1.

(B) Wash the residue obtained in the previous test three times with successive small quantities of *water*. To the residue add 5 ml of *dilute hydrochloric acid*, filter, and add to the filtrate 0.3 ml of *dilute sulphuric acid*. A white precipitate is formed which is insoluble in *dilute hydrochloric acid*.

Acidity or Alkalinity : Heat 5 g with 20 ml of freshly boiled and cooled *water* on a water-bath for five minutes and filter. To 10 ml of the filtrate add one drop of *bromothymol blue solution*. Not more than 0.5 ml of *0.01N hydrochloric acid* or *0.01N sodium hydroxide* is required to change the colour of the solution.

Phosphate : Boil 1 g with a mixture of 3 ml of *nitric acid* and 5 ml of *water* for five minutes, and add *water* to restore the original volume. Filter through a filter paper previously washed with *dilute nitric acid*. Add to the warm filtrate an equal volume of *ammonium molybdate solution*; no yellow precipitate is formed.

Arsenic : Not more than 1 part per million, Appendix 3.2.1.

Heavy metals : Not more than 10 parts per million, determined by Method A on the solution prepared by the following method: Boil 4 g with a mixture of 2 ml of *glacial acetic acid* and 48 ml of *water* for ten minutes. Add *water* to make 50 ml, filter, reject the first five ml of the filtrate. Use 25 ml of the filtrate for the test, Appendix 3.2.4.

Sulphide : Boil 10 g with a mixture of 10 ml of *dilute hydrochloric acid* and 90 ml of *water* for ten minutes. Expose to the vapour, *lead acetate paper*; the paper does not darken.

Acid-soluble substances : Not more than 0.3 per cent, determined by the following method: Cool the mixture obtained in the test for sulphide, add *water* to restore the original volume, and filter through paper, previously washed with a mixture of 10 ml of *dilute hydrochloric*

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

acid and 90 ml of *water*, returning the first portions, if necessary, to obtain a clear filtrate. Evaporate 50 ml of the filtrate on a water-bath to dryness, and add two drops of *hydrochloric acid* and 10 ml of hot *water*. Filter again through acid-washed paper, prepared as directed above, wash the filter with 10 ml of hot *water*, and evaporate the combined filtrate and washings; dry the residue at 105°, cool and weigh.

Soluble barium salts : Digest the residue obtained in the test for acid-soluble substances with 10 ml of *water* and filter through a paper previously washed with a mixture of 10 ml of *dilute hydrochloric acid* and 90 ml of *water*. Add 0.5 ml of *dilute sulphuric acid* to the clear filtrate and set aside for thirty minutes; no turbidity is produced.

Bulkiness : Place 5.0 g in a glass-stoppered 50-ml graduated cylinder and having the 50 ml graduation mark 14 cm from the base. Add *water* to 50 ml, shake the mixture for five minutes, and allow to stand for fifteen minutes. The Barium Sulphate does not settle below the 15 ml mark.

Assay : Weigh accurately about 0.60 g in a platinum crucible, add 5 g of *sodium carbonate* and 5 g of *potassium carbonate* and mix. Heat to 1000° and maintain at this temperature for fifteen minutes. Allow to cool and suspend the residue in 150 ml of *water*. Wash the dish with 2 ml of *acetic acid* and add to the suspension. Cool in ice and filter by decantation, transferring as little of the solid matter as possible to the filter. Wash the residue with successive quantities of a 2 per cent w/v solution of *sodium carbonate* until the washings are free from sulphate; discard the washings. Add 5 ml of *dilute hydrochloric acid* to the filter, and wash through into the vessel containing the bulk of the solid matter with *water*. Add 5 ml of *hydrochloric acid* and dilute to 100 ml with *water*. Add 10 ml of a 40 per cent w/v solution of *ammonium acetate*, 25 ml of a 10 per cent w/v solution of *potassium dichromate* and 10 g of *urea*. Cover, and digest in a hot-air oven at 80° to 85° for sixteen hours; filter whilst still hot through a sintered glass filter (grade 4, maximum pore size 10 µm), washing the precipitate initially with a 0.5 per cent w/v solution of *potassium dichromate* and finally with 2 ml of *water*. Dry to constant weight at 105°. 1.0 g of the residue is equivalent to 0.9213 g of barium sulphate, $BaSO_4$.

Storage : Store in well-closed containers.

Barium Sulphate for Suspension

Barium Meal

Category : Diagnostic aid (radio-opaque medium).

Description : White or coloured fine powder or granules.

Standards : Barium Sulphate for Suspension is a dry mixture of Barium Sulphate with suitable flavours, colours, preservatives and suspending/dispersing agents. It contains not less than 90.0 per cent of $BaSO_4$.

Identification : Ignite 1.0 g to constant weight. The residue complies with **Identification** tests (A) and (B) described under Barium Sulphate.

pH : Between 4.0 and 8.0, determined in a 60 per cent w/w suspension in *water*, Appendix 5.10.

Soluble barium compounds : To 10 g of an aqueous suspension containing 75 per cent w/v of Barium Sulphate add 10 ml of *dilute hydrochloric acid* and 90 ml of *water*. Boil for ten minutes, cool, and filter. Wash the residue with *water* and dilute the combined filtrate and washings to 100 ml with *water*. Carefully evaporate 50 ml of the resulting solution to avoid charring, add 2 drops of *dilute hydrochloric acid* and 10 ml of hot *water* to the residue, and filter. To the clear filtrate add 0.5 ml of *dilute sulphuric acid* and allow to stand for thirty minutes, no turbidity is produced.

Water stability : To 80 ml of *water* contained in a Crow receiver, add 20 ml of an aqueous suspension of the substance being examined, containing 75 per cent w/v of Barium Sulphate. Mix thoroughly, allow to stand for twenty-four hours, and decant the supernatant liquid; the volume of sediment is not greater than 5.0 ml.

Acid stability : Carry out the test for **Water stability**, using 20 ml of *0.1 N hydrochloric acid* and 60 ml of *water* instead of 80 ml of *water*. The volume of sediment is not greater than 5.0 ml and does not exceed the figure obtained in the test for **Water stability** by more than 2.5 ml.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying at 105° for four hours, Appendix 5.8.

Assay : Weigh accurately about 0.75 g in a platinum dish and complete the **Assay** described under Barium Sulphate beginning at the words "add 5 g of *sodium corbonate*.....".

Storage : Store in well-closed containers.

White Beeswax

Category : Pharmaceutical aid (stiffening agent).

Description : Yellowish-white solid, somewhat translucent in thin layers; odour, faint and characteristic.

Solubility : Practically insoluble in *water*; sparingly soluble in cold *alcohol*; soluble in *chloroform*, in warm *solvent ether* and in fixed and volatile oils.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Standards : White Beeswax is the product of bleaching Yellow Beeswax that is obtained from the honeycomb of the bee, *Apis mellifera* L., and other species of *Apis*.

Melting range : Between 62° and 65°, determined by Method II, Appendix 5.11.

Acid value : Between 5 and 10, Appendix 3.3.15, determined by the following method: Weigh accurately about 5 g and dissolve in 20 ml of boiling *ethyl alcohol*, previously neutralised to *phenolphthalein solution*, and titrate with *0.5N alcoholic potassium hydroxide*, using *phenolphthalein solution* as indicator.

Ester value : Between 80 and 95, determined by subtracting the *acid value* from the *saponification value*. The *saponification value*, Appendix 3.3.20, is determined by boiling 5 g for one and a quarter hours with 25 ml of *N alcoholic potassium hydroxide* prepared with *ethyl alcohol*, and titrating, while hot, with *N hydrochloric acid*, using *phenolphthalein solution* as indicator.

Ratio-number : Between 8 and 19, determined by dividing the *ester value* by the *acid value*.

Fats; Fatty acids; Japan wax and resin : Boil 5 g for ten minutes with 80 ml of 10 per cent w/v solution of *sodium hydroxide*, replace the water lost by evaporation, cool; filter the solution through glass wool, or asbestos, and acidify with *hydrochloric acid*, no precipitate is produced.

Saponification cloud test : Place 3.0 g in a 100 ml boiling flask fitted with a ground-glass joint. Add 30 ml of a solution prepared by dissolving 40 g of *potassium hydroxide* in about 900 ml of *aldehyde-free alcohol* maintained at a temperature not exceeding 15°, and then when solution is complete, warming to room temperature and adding *aldehyde-free alcohol* to make 1000 ml. Boil the mixture gently under a reflux condenser, for two hours. Detach the flask from the condenser, insert a thermometer into the solution, and place the flask in a container of water at a temperature of 80°. Rotate the flask in the bath while both the bath and the solution cool; the solution shows no cloudiness or globule formation before the temperature reaches 62°.

Storage : Store in well-closed containers.

Yellow Beeswax

Category : Pharmaceutical aid (stiffening agent).

Description : Yellow to greyish-brown solid, somewhat brittle when cold; odour, faint and characteristic.

Solubility : Practically insoluble in *water*; sparingly soluble in *alcohol* and *solvent ether*; soluble in *chloroform* and in fixed and volatile oils.

Standards : Yellow Beeswax is the purified wax that is obtained from the honeycomb of the bee, *Apis meilifera* L., and other species of *Apis*.

Melting range; Acid value; Ester value; Ratio number; Fats; Fatty acids; Japan wax and resin; Saponification cloud test : Complies with the requirements stated under White Beeswax.

Storage : Store in well-closed containers.

Belladonna Herb

Belladonna Leaf

Category : Anticholinergic.

Standards : Belladonna Herb consists of the dried leaf or of the dried leaf and flowering tops of *Atropa belladonna* Linn. or of *Atropa acuminata* Royle ex Lindley (Fam. Solanaceae) or a mixture of both species. It contains not less than 0.30 per cent of total alkaloids, calculated as hyoscyamine with reference to the herb dried at 100° to 105°.

Description : The leaves are green to greenish-brown, slightly darker on the upper surface, often crumpled and rolled and partly matted together in the drug. When whole, the lamina is 5 to 25 cm long and 3 to 12 cm wide, elliptical to ovate: acuminate at the apex, narrowing at the base; margin, entire. Petiole 0.5 to 4 cm in length. The young leaves are highly pubescent, the older leaves are slightly pubescent along the veins. Seen under a lens magnifying to at least 6 diameters, microsphenoidal crystal cells are visible between the veins as dark points by transmitted light and as bright points by reflected light.

In the flowering tops, the stems are hollow and flattened, with leaves in pairs of unequal size, in the axils of which are single flowers with campanulate corolla, about 2 cm long and 1.5 cm wide, purple or yellow-brown in colour, with five short, reflexed lobes, five epipetalous stamens and one superior bilocular ovary with numerous ovules.

Odour, slightly nauseous; taste, unpleasant and slightly bitter.

Examined under a microscope it shows epidermal cells with sinuate anticlinal walls and cuticle which is often striated and furrowed. Covering and

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

glandular hairs infrequent though more frequent in the young leaves and around the veins; covering hairs, multicellular, uniseriate, with thin smooth walls; glandular hairs; short clavate glands with multicellular heads and glands with a long uniseriate stalk and ovoid unicellular head. Stomata, anisocytic, more frequent on the lower epidermis. The midrib is characterised by an open arc of vascular bundles with isolated groups of perimedullary phloem. Mesophyll dorsiventral with a single palisade layer. Throughout the parenchyma and particularly just below the palisade layer are cells containing microsphenoidal crystals of calcium oxalate or, very rarely, cluster crystals.

The stems show pericyclic fibres and perimedullary bundles of phloem, few trichomes; the cortical parenchymatous cells and the pith cells contain microsphenoidal crystals of calcium oxalate.

Identification : Powder 1 g and shake for two minutes with 10 ml of *0.1N sulphuric acid.* Filter and add to the filtrate 1 ml of *strong ammonia solution* and 5 ml of *water.* Extract with 15 ml of *solvent ether,* taking care to prevent the formation of an emulsion. Dry the ether extract over *anhydrous sodium sulphate* and filter. Evaporate the filtrate to dryness, add ten drops of *fuming nitric acid* and evaporate to dryness. Add 10 ml of *acetone* and, dropwise, a 3 per cent w/v solution of *potassium hydroxide* in *alcohol.* A deep violet colour develops.

Foreign organic matter : Not more than 3.0 per cent, Appendix 3.3.22.

Sulphated ash : Not more than 18.0 per cent, Appendix 3.2.7.

Acid-insoluble ash : Not more than 3.0 per cent, Appendix 3.3.22.

Assay : Powder 50 g and determine the loss on drying by drying 2.0 g, accurately weighed, in an oven at 100° to 105°. From the remaining sample weigh accurately about 10 g, moisten with a mixture of 5 ml of *dilute ammonia solution,* 10 ml of *alcohol* and 30 ml of *solvent ether* and mix thoroughly. Transfer the mixture to a percolator with the aid of an extracting solvent mixture consisting of 3 volumes of *solvent ether* and 1 volume of *chloroform.* Allow to macerate for four hours and percolate with the solvent mixture until *complete extraction* of the alkaloids is effected, Appendix 3.3.22.

Concentrate the percolate to about 50 ml by distilling off the solvent mixture on a water-bath, and transfer to a separator, previously rinsed with *solvent ether.* Add a quantity of *solvent ether* at least equal to 2.1 times the volume of the percolate and extract with three quantities, each of 20 ml, of *0.5N sulphuric acid.* Transfer each acid extract to another separating funnel. Combine the acid extracts, make the solution alkaline with *dilute ammonia solution* and extract with *chloroform,* until *complete extraction* of the alkaloids has been effected. Wash the combined chloroform extracts with 10 ml of *water,* discard the water, evaporate the chloroform layer to dryness and heat the residue for fifteen minutes on a water-bath. Redissolve the residue in successive small quantities of *chloroform,* evaporating to dryness on a water-bath each time before adding the solvent. Heat for fifteen minutes on a water-bath and dissolve the residue in 5 ml of *chloroform.* Add 20.0 ml of *0.02N sulphuric acid,* remove the chloroform by evaporation on a water-bath and titrate the excess of acid with *0.02N sodium hydroxide* using *methyl red solution* as indicator. Each ml of *0.02N sulphuric acid* is equivalent to 0.005788 g of total alkaloids calculated as hyoscyamine. Calculate the content of total alkaloids with reference to the dried substance.

Storage : Store in tightly-closed, light-resistant containers protected from moisture.

BELLADONNA HERB POWDER

Description : Fairly dark green fragments of epidermis made up of cells with sinuous walls and sinuous striated cuticle, with numerous anisocytic stomata. Few covering hairs and glandular hairs, fragments of parenchyma with cells containing microsphenoidal crystals of calcium oxalate from 0.5 μm to several μm in size; they are also found scattered throughout the powder and glitter when viewed under polarising microscope A few fibres from the stem and occasionally a few subspherical grains of pollen, about 40 μm in size, are present.

Foreign organic matter; Sulphated ash; Acid-insoluble ash; Assay : Complies with the requirements stated under Belladonna Herb.

Storage : Store in tightly-closed, light-resistant containers, protected from moisture.

Belladonna Dry Extract

Belladonna Extract

Category : Anticholinergic.

Dose : 15 to 60 mg.

Standards : Belladonna Dry Extract is a dried and powdered, alcoholic percolate of Belladonna Herb, adjusted to contain not less than 0.95 per cent and not more than 1.05 per cent of the alkaloids of Belladonna Herb, calculated as hyoscyamine. It may be prepared in the following manner:

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Percolate 1000 g of Belladonna Herb in *moderately coarse powder* with *alcohol (70 per cent)* or Industrial Methylated Spirit until 4000 ml of percolate has been obtained. Evaporate 20 ml of the percolate, dry the residue at 80°, weigh and determine the proportion of total solid in the percolate. Determine also the proportion of alkaloids in the percolate and in the Belladonna Herb in *fine powder*. From the results of the three determinations, calculate the amount of Belladonna Herb in *fine powder* that must be added to the percolate to produce a dry extract containing 1.0 per cent of alkaloids.

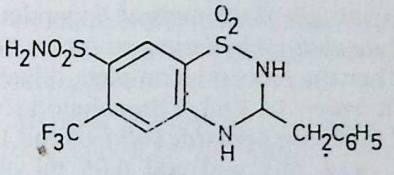
Add to the percolate a somewhat smaller amount of Belladonna Herb in *fine powder* than calculation has shown to be necessary, evaporate the alcohol and evaporate the residue to dryness under reduced pressure at a temperature not exceeding 60°, and dry in a current of air at 80° Powder the residue, add the final necessary amount of Belladonna Herb in fine powder and triturate in a dry, slightly warmed mortar until thoroughly mixed. Pass the Extract through a *sieve No. 22* and mix.

Assay : Weigh accurately about 3 g and wash into a separator with 12 ml of a mixture of equal volumes of *alcohol* and *water*, shake well and frequently during about thirty minutes, add 2 ml of *dilute ammonia solution* and 25 ml of *chloroform*. Shake well, allow to separate and filter the chloroform layer into a second separator through a plug of cotton wool previously moistened with *chloroform*. Continue the extraction with further quantities, each of 25 ml, of *chloroform* until *complete extraction* of the alkaloids is effected, Appendix 3.3.22, running each chloroform solution through the same plug of cotton wool. Extract the combined chloroform solutions with successive quantities of a mixture of 3 volumes of *0.2N sulphuric acid* and 1 volume of *alcohol* until *complete extraction* of the alkaloids is effected, filtering each extract through a plug of cotton wool previously moistened with *water*. Wash the mixed acid solutions with 10, 5 and 5 ml of *chloroform*, extracting each chloroform solution with the same 20 ml of *0.1N sulphuric acid* and rejecting the chloroform. Combine the acid solutions, neutralise with *dilute ammonia solution*, add 5 ml in excess, and shake with successive quantities, each of 25 ml of *chloroform* until *complete extraction* of the alkaloids is effected, washing each chloroform solution with the same 10 ml of *water* and filtering into a flask through a plug of cotton wool previously moistened with *chloroform*. Distil most of the chloroform from the combined extracts and transfer the remainder of the solution to a shallow open dish. Evaporate the remainder of the chloroform without the aid of a current of air, heat the residue in an oven at 100° for fifteen minutes, dissolve in a little *chloroform*, evaporate to dryness without the aid of a current of air, and again heat in an oven at 100° for fifteen minutes. Dissolve the residue in 2 ml of *chloroform*, add 50 ml of *0.05N sulphuric acid*, warm to remove the chloroform, cool, and titrate the excess of acid with *0.05N sodium hydroxide*, using *methyl red solution* as indicator. Each ml of *0.05N sulphuric acid* is equivalent to 0.01447 g of alkaloids calculated as hyoscyamine.

Storage : Store in small, wide-mouthed, well-closed containers in a cool place.

Bendrofluazide

Bendroflumethiazide



$C_{15}H_{14}F_3N_3O_4S_2$ Mol. Wt. 421.41

Category : Diuretic, anti-hypertensive.

Dose : Diuretic, initial, 5 to 20 mg daily, maintenance, 2.5 to 5 mg daily. Anti-hypertensive, initial, 5 to 20 mg daily, maintenance, 2.5 to 50 mg daily.

Description : White to cream-coloured crystalline powder; odourless or almost odourless; tasteless.

Solubility : Freely soluble in *acetone*; soluble in *alcohol*; insoluble in *water* and in *chloroform*.

Standards : Bendrofluazide is 3-benzyl-3, 4-dihydro-6-trifluoromethyl-2*H*-1, 2, 4-benzothiadiazine-7-sulphonamide 1, 1-dioxide. It contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of $C_{15}H_{14}F_3N_3O_4S_2$, calculated with reference to the dried substance.

Identification : (A) Dissolve 10 mg in 10 ml of *0.1N sodium hydroxide*, add sufficient *water* to produce 100 ml and dilute 10 ml to 100 ml with *0.01N sodium hydroxide*. The light absorption, in the range 230 to 350 nm of a 1-cm layer of the resulting solution exhibits two maxima, at 273 nm and 329 nm; *extinction* at 273 nm, about 0.42 and at 329 nm, about 0.08, Appendix 5.15A.

(B) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 5 volumes of *benzene*, 3 volumes of *solvent ether* and 2 volumes of *acetone* as the mobile phase. Apply separately to the plate 20 µl of each of two solutions in *methyl alcohol*

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

containing (1) 0.02 per cent w/v of substance being examined and (2) 0.02 per cent w/v of *bendrofluazide R.S.* respectively. After removal of the plate allow it to dry in air until the odour of the solvent is no longer detectable, and spray the dried plate with a 10 per cent v/v solution of *sulphuric acid* in *alcohol*, heat at 105° for 30 minutes, and immediately expose to nitrous fumes in a closed glass tank for 15 minutes [nitrous fumes may be generated by adding *sulphuric acid (50 per cent w/w)* dropwise to a solution containing 10 per cent w/v of *sodium nitrite* and 3 per cent w/v of *potassium iodide*]. Place the plate in a current of warm air for fifteen minutes and spray with a 0.5 per cent solution of w/v *N-(1-naphthyl) ethylenediamine hydrochloride* in *alcohol*. If necessary allow to dry, and repeat the spraying. The principal spot in the chromatogram obtained with solution (1) corresponds in colour and intensity to that in the chromatogram obtained with solution (2).

(C) Burn 20 mg by the *oxygen flask method*, Appendix 3.3.6, using 5 ml of *dilute sodium hydroxide solution* as the absorbing liquid. When the process is complete, dilute the liquid to 25 ml with *water*. To 5 ml of the solution so obtained, add 0.1 ml of *hydrogen peroxide solution* and 1 ml of *N hydrochloric acid*, mix and add 0.05 ml of *barium chloride solution*; a turbidity is produced. To a further 0.2 ml of the solution, obtained as described above, add 0.5 ml of *alizarin fluorine blue solution*, sufficient *0.02N hydrochloric acid* to give a full yellow colour and *0.02N sodium hydroxide* drop by drop until the solution just begins to turn pink. Add 0.2 ml of a solution containing 12 per cent w/v of *sodium acetate* and 6 per cent v/v of *glacial acetic acid*, dilute with *water* to 4 ml, and add 0.5 ml of *cerous nitrate solution*; a deep lilac-blue colour is produced.

(D) Warm 20 mg with *a strong potassium permanganate solution* acidified with *sulphuric acid*; benzaldehyde, recognisable by its odour, is produced (distinction from hydroflumethiazide).

Free amine : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel HF 254* as the coating substance and *solvent ether* as the mobile phase. Apply separately to the plate 2µl of each of two solutions in *acetone* containing (1) 5.0 per cent w/v of the substance being examined and (2) 0.05 per cent w/v of *5-trifluoromethyl -2, 4-disulphamoylaniline. R.S.* After removal of the plate, dry it in a current of air, and examine under an ultra-violet lamp having a maximum output at about 254 nm. The spot in the chromatogram obtained with solution (2) is more intense than any corresponding spot in the chromatogram obtained with solution (1).

Heavy metals : Not more than 20 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Assay : Weigh accurately about 0.2 g and dissolve in 50 ml of *pyridine* in a tall beaker. Add three drops of a saturated solution of *azo violet* in *benzene*, cover the beaker and gently bubble *nitrogen* through the solution for five minutes, taking care to avoid any contact between the solution and the cover. Raise the nitrogen delivery tube above the surface of the solution and continue to pass *nitrogen*. Stir the solution and titrate with *0.1N sodium methoxide* from a burette passing through an opening in the cover. Titrate to a blue end-point. Carry out a blank determination and make any necessary correction. Each ml of *0.1N sodium methoxide* is equivalent to 0.02107 g of $C_{15}H_{14}F_3N_3O_4S_2$.

Storage : Store in tightly-closed containers.

Bentonite

Category : Pharmaceutical aid (suspending agent).

Description : Very fine, pale buff, or cream-coloured to greyish-white powder, free from grit; odourless; taste, slightly earthy.

Solubility : Insoluble in *water* but swells into a homogeneous mass; insoluble in, and does not swell in organic solvents.

Standards : Bentonite is a natural, colloidal, hydrated aluminium silicate.

Identification : Fuse 1 g with 2 g of *anhydrous sodium carbonate*, warm the residue with 10 ml of *water*, filter, wash the filter with 5 ml of *water*, and reserve the combined filtrate and washings. Dissolve the residue in 10 ml of *dilute hydrochloric acid*; the solution gives the reactions of *aluminium*. Appendix 3.1. Add to the reserved filtrate and washings 3 ml of *hydrochloric acid*; a gelatinous precipitate is produced.

pH : Between 9.0 and 10.5, determined in a 2.0 per cent w/v suspension in *water*, Appendix 5.10.

Sedimentation volume : In a mortar, mix 6 g with 0.3 g of *light magnesium oxide*, freshly calcined. Mix the powder progressively with 200 ml of *water*. Shake for 1 hour and place 100 ml of the suspension in a 100-ml graduated cylinder. After 24 hours the volume of the clear supernatant liquid is not greater than 2 ml.

Swelling powder : Add 2.0 g in twenty portions at intervals of 2 minutes to 100 ml of a 1 per cent w/v solution of *sodium laurylsulphate* in a 100-ml graduated cylinder about 3 cm in diameter. Allow each portion to settle before adding the next. Allow to stand for 2 hours. The apparent volume of the sediment at the bottom of the cylinder is not less than 24 ml.

Coarse particles : Triturate 5.0 g with successive quantities of *sodium hexametaphosphate solution* and

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

transfer to a 500-ml graduated cylinder about 5 cm in diameter. Shake vigorously until the agglomerates have dispersed; allow to stand for thirty minutes, shake again for a few minutes, and allow to stand for twenty-four hours. Re-suspend the contents of the cylinder and allow to stand for two hours.

Construct a syphon system consisting of glass tubing of 5 mm internal diameter constricted at the inlet to an orifice 2.5 mm in diameter. Connect the lower, outlet end of the tube to a 6-cm length of capillary tubing, 1 mm in bore, with a 4-cm length of rubber tubing fitted with a tubing clamp. Fill the system with *water*, close the clamp, insert the tube in the cylinder so that the inlet is 4 cm above the bottom of the cylinder and syphon off the colloidal suspension.

Suspend the residue in 400 ml of *water* and transfer to a *sieve* of nominal mesh aperture 125 µm, previously dried at 100° to 105° and weighed, placed on a suitable funnel. If the clay-like fraction is sufficient to cause a slight blockage, transfer in two portions and wash the sieve with *water* between the two operations in order to eliminate the clay-like fraction. Wash the cylinder with several large quantities of *water*. Pour the washings into a 600-ml conical flask and transfer to the sieve. Wash the flask and sieve with 100 ml of *water*. Dry the sieve at 100° to 105° and weigh; the weight of the particles on the sieve is not more than 5 mg.

Loss on drying : Between 5.0 and 12.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Storage : Store in tightly-closed containers.

Benzalkonium Chloride Solution

Category : Pharmaceutical aid (antiseptic detergent).

Description : Clear, colourless or slightly yellow, syrupy liquid; odour, aromatic; taste, very bitter.

Solubility : Miscible with *water* and with *alcohol*.

Standards : Benzalkonium Chloride Solution is a solution of a mixture of alkylbenzyldimethylammonium chlorides. It contains not less than 49.0 per cent w/v and not more than 51.0 per cent w/v of alkylbenzyldimethylammonium chlorides, calculated as $C_{22}H_{40}ClN$. It may contain not more than 16.0 per cent v/v of Alcohol.

Identification : (A) Dilute 0.2 ml with 10 ml of *water*. To 5 ml add 1.5 ml of *dilute nitric acid*; a white precipitate is produced which is soluble in *alcohol*. To the remainder add 1.5 ml of *mercuric chloride solution*; a white precipitate is produced which is soluble in *alcohol*.

(B) Evaporate 0.5 ml to dryness on a water-bath, dissolve the residue in 1 ml of *sulphuric acid*, add 0.1 g of *potassium nitrate*, heat on a water-bath for five minutes, cool, dilute with *water* to 10 ml, add 0.5 g of *zinc powder*, and heat on a water-bath for five minutes. To 2 ml of the clear supernatant liquid add 0.5 ml of *sodium nitrite solution*, cool in ice and add to 3 ml of *β-naphthol solution*; an orange-red colour is produced.

(C) A solution in *water* is neutral or slightly alkaline to *litmus solution*, and foams strongly on shaking.

(D) A solution (1 in 10) gives the reactions of *chlorides*, Appendix 3.1.

Ammonia compounds : Boil 0.2 ml with 3 ml of *sodium hydroxide solution*; no odour of ammonia is produced.

Foreign amines : To a volume equivalent to 0.1 g of Benzalkonium Chloride add sufficient *water* to produce 5 ml and add 3 ml of *N sodium hydroxide*; no precipitate is formed. Heat to boiling; the odour of amines is not perceptible.

Alcohol (if present) : Not more than 16.0 per cent v/v, determined by *gas-liquid chromatographic Method I or II*, as applicable, Appendix 5.28.

Sulphated ash : Not more than 0.2 per cent, Appendix 3.2.7.

Assay : Dissolve 4 g in sufficient *water* to produce 100.0 ml. Transfer 25.0 ml to a separating funnel, add 25 ml of *chloroform*, 10 ml of *0.1N sodium hydroxide*, and 10.0 ml of a freshly prepared 5 per cent w/v solution of *potassium iodide*. Shake well, allow to separate, and run off the chloroform layer. Shake the aqueous solution with three further quantities, each of 10 ml, of *chloroform*, and discard the chloroform solution. Add 40 ml of *hydrochloric acid*, cool and titrate with *0.05M potassium iodate* until the solution becomes pale brown in colour. Add 2 ml of *chloroform* and continue the titration until the chloroform becomes colourless. Titrate a mixture of 20 ml of *water*, 10.0 ml of the *potassium iodide solution* and 40 ml of *hydrochloric acid* with *0.05M potassium iodate* in a similar manner; the differences between the titrations represent the amount of *0.05M potassium iodate* required. Each ml of *0.05M potassium iodate* is equivalent to 0.0354 g of $C_{22}H_{40}ClN$. Determine the *weight per ml*, Appendix 5.19, and calculate the amount of $C_{22}H_{40}ClN$, weight in volume.

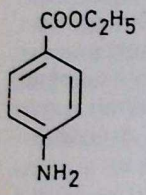
NOTE—Benzalkonium Chloride Solution may contain, in place of Alcohol, specially Denatured Spirit, diluted so as to be of equivalent alcoholic strength.

Storage : Store in tightly-closed, light-resistant containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Benzocaine



$C_9H_{11}NO_2$ Mol. Wt. 165.19

Category : Local anaesthetic.

Description : Colourless crystals, or white, crystalline powder; odourless; taste, bitter, followed by local anaesthesia of the tongue.

Solubility : Very slightly soluble in *water*; freely soluble in *alcohol*, in *chloroform* and in *solvent ether*; soluble in dilute acids.

Standards : Benzocaine is ethyl 4-aminobenzoate. It contains not less than 99.0 per cent of $C_9H_{11}NO_2$, calculated with reference to the dried substance.

Identification : (A) Dissolve 10 mg in 1 ml of *water* with the aid of one drop of *dilute hydrochloric acid*, and add 2 drops of a 10 per cent w/v solution of *sodium nitrite* and 2 drops of a solution of 10 mg of *β-naphthol* in 5 ml of *sodium hydroxide solution*; a deep red colour is produced; on setting aside the solution for some time a scarlet precipitate is produced.

(B) Dissolve 0 2 g in 10 ml of *water* with the aid of *dilute hydrochloric acid* and divide into two parts.

(a) To one part add *iodine solution*; a precipitate is obtained (distinction from orthocaine)

(b) To the other part add *potassium mercuri-iodide solution* no precipitate is obtained (distinction from procaine hydrochloride)

Melting range : Between 88° and 92°, Appendix 5.11.

Acidity or Alkalinity : Dissolve 0.5 g in 5 ml of *alcohol*, add 10 ml of *water* and one drop of *phenolphthalein solution*. No pink colour is produced. Add 0.5 ml of *0.01N sodium hydroxide*, the solution develops a pink colour.

Heavy metals : Not more than 10 parts per million, determined on 2.0 g by Method B, Appendix 3.2.4.

Chloride : Dissolve 0.2 g in 5 ml of *alcohol*, previously acidified with a few drops of *dilute nitric acid* and add a few drops of *silver nitrate solution*; no turbidity is produced immediately.

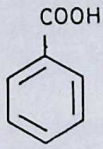
Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying "in vacuo", Appendix 5.8.

Assay : Weigh accurately about 0.4 g and dissolve in a mixture of 25 ml of *hydrochloric acid* and 50 ml of *water*. Cool to 10° and carry out the *nitrite titration*, Appendix 3.3.4. Each ml of *0.1M sodium nitrite* is equivalent to 0.01652 g of $C_9H_{11}NO_2$.

Storage : Store in well-closed, light-resistant containers.

Benzoic Acid



$C_7H_6O_2$ Mol. Wt. 122.12

Category : Pharmaceutical aid (antifungal and antibacterial agent).

Description : Colourless, light, crystals, scales or needles; odour, slight and characteristic.

Solubility : Slightly soluble in *water*; freely soluble in *alcohol* in *chloroform* and in *solvent ether*.

Standards : Benzoic Acid contains not less than 99.5 per cent and not more than the equivalent of 100.5 per cent of $C_7H_6O_2$, calculated with reference to the anhydrous substance.

Identification : (A) Warm gently 0.2 g with 20 ml of *water* and add 1 ml of *N sodium hydroxide* and filter. To the filtrate add *ferric chloride test-solution*; a buff coloured precipitate is produced.

(B) A solution is acid to *methyl red solution*.

(C) The light absorption, in the range 220 to 350 nm, of a 1-cm layer of a 0.001 per cent w/v solution in *methyl alcohol* exhibits a maximum only at 225 nm; *extinction* at 225 nm, about 0.8, Appendix 5.15A.

Melting range : Between 121° and 123°, Appendix 5.11.

Arsenic : Not more than 2 parts per million, Appendix 3.2.1.

Heavy metals : Not more than 10 parts per million, determined by the following method: Dissolve 2.0 g in 25 ml of *acetone*; and add 2 ml of *water* and 10 ml of *hydrogen sulphide solution*; any colour produced is not darker than that of a control made with 25 ml of *acetone*, 2.0 ml of *standard lead solution* and 10 ml of *hydrogen sulphide solution*.

Readily oxidisable substances : Add 1.5 ml of *sulphuric acid* (containing 94.5 per cent to 95.5 per cent w/w of H_2SO_4) to 100 ml of *water*, heat to boiling, add drop by drop *0.1N potassium permanganate* until the pink colour persists for thirty seconds. Dissolve

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

exactly 1 g of benzoic acid in the hot solution and titrate with *0.1 N potassium permanganate* to a pink colour that persists for fifteen seconds; not more than 0.5 ml of *0.1 N potassium permanganate* is required.

Cinnamic acid : Warm 0.1 g with 0.1 g of *potassium permanganate*, and 5 ml of *dilute sulphuric acid*; no odour of benzaldehyde is developed.

Chlorinated compounds : Dissolve 0.5 g in 5 ml of *N sodium carbonate*, evaporate to dryness, and heat the residue until completely charred, keeping the temperature below 400° Extract the residue with a mixture of 10 ml of *water* and 12 ml of *dilute nitric acid*, and filter; the filtrate complies with the *limit test for chlorides*, Appendix 3.2.2.

Readily carbonisable substances : Dissolve 0.50 g in 5 ml of *sulphuric acid* (containing 94.5 per cent to 95.5 per cent w/w of H_2SO_4), the solution has no more colour than that of a mixture of 0.2 ml of *cobalt chloride C.S.*, 0.3 ml of *ferric chloride C.S.*, and 0.1 ml of *copper sulphate C.S.* and 4.4 ml of *water.*

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Water : Not more than 0.7 per cent w/w, using a mixture of one volume of *methyl alcohol* and two volumes of *pyridine* as the solvent, Appendix 3.3.25.

Assay : Weigh accurately, about 2.5 g and dissolve in 15 ml of warm *alcohol* previously neutralised to *phenolphthalein solution*. Add 20 ml of *water* and titrate with *0.5 N sodium hydroxide*, using *phenolphthalein solution* as indicator. Each ml of *0.5 N sodium hydroxide* is equivalent to 0.06106 g of $C_7H_6O_2$

Storage : Store in well-closed containers.

Compound Benzoic Acid Ointment

Benzoic and Salicylic Acid Ointment, Whitfield's Ointment

Category : Antifungal (topical).

Standards : Compound Benzoic Acid Ointment is Benzoic Acid and Salicylic Acid present in the ratio of 2 to 1 in a base consisting of a mixture of 3 parts of Emulsifying Wax, 5 parts of White Soft Paraffin and 2 parts of Liquid Paraffin or in any other suitable ointment base. It contains not less than 5.7 per cent and not more than 6.3 per cent w/w of Benzoic Acid, $C_7H_6O_2$, and not less than 2.85 per cent and not more than 3.15 per cent w/w of Salicylic Acid, $C_7H_6O_3$.

Identification : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3 using a suitable grade of silica gel as the coating substance and a mixture of 90 volumes of *benzene*, 16 volumes of *methyl alcohol* and 18 volumes of *glacial acetic acid* as the mobile phase. Apply separately to the plate 10 µl of each of the following solutions: (1) 0.66 per cent w/v of the ointment in *chloroform*; (2) a solution of 40 mg of *benzoic acid R.S.* and 20 mg of *salicylic acid R.S.* in 100 ml of *chloroform.* After removal of the plate allow it to dry in air and examine under an ultra-violet lamp having a maximum output at about 254 nm. The two major fluorescent spots in chromatogram obtained with solution (1) corresponds to the ones in the chromatogram obtained with solution (2).

Assay : (1) *For benzoic acid* – Weigh accurately about 2.5 g and dissolve with the aid of gentle heat, as completely as possible in 50 ml of a mixture of equal volumes of *alcohol* and *solvent ether*, previously neutralised to *phenolphthalein solution*, and titrate with *0.1 N sodium hydroxide* using *phenolphthalein solution* as indicator. Each ml of *0.1 N sodium hydroxide*, after deducting 1 ml for each 0.01381 g of $C_7H_6O_3$ in the weight of the ointment taken (calculated from the result of the **Assay** *for salicylic acid*) is equivalent to 0.01221 g of $C_7H_6O_2$

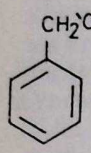
(2) *For salicylic acid* – Weigh accurately about 2.5 g and dissolve with the aid of gentle heat, as completely as possible in 50 ml of *solvent ether*, and extract with five quantities, each of 10 ml, of a saturated solution of *sodium bicarbonate*, washing each extract with the same 50 ml of *solvent ether.* Combine the aqueous extracts, cautiously add *hydrochloric acid* until the solution is distinctly acid to *litmus paper* and extract with four quantities, each of 25 ml of *solvent ether*; combine the extracts and evaporate the ether at a temperature below 40°. Dissolve the residue in 5 ml of *0.5 N sodium hydroxide*, add 50.0 ml of *0.1 N bromine* and 5 ml of *hydrochloric acid*, shake repeatedly during fifteen minutes, and allow to stand for fifteen minutes. Add 10 ml of *potassium iodide solution* and titrate with *0.1 N sodium thiosulphate* using *starch solution* added towards the end of the titration, as indicator. Repeat the operation without the substance being examined. The difference between the titrations represents the amount of bromine required. Each ml of *0.1 N bromine* is equivalent to 0.002302 g of $C_7H_6O_3$

Storage : Store in well-closed containers at a temperature not exceeding 30°.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Benzyl Alcohol



C_7H_8O Mol. Wt. 108.14

Category : Local anaesthetic; antiseptic.

Description : Colourless liquid; almost odourless; taste, sharp and burning.

Solubility : Soluble in *water*; miscible with *alcohol*, with *chloroform*, and with *solvent ether*.

Standards : Benzyl Alcohol contains not less than 97.0 per cent w/w of C_7H_8O.

Identification : Add three drops to a strong *potassium permanganate solution* acidified with *sulphuric acid*; benzaldehyde, recognisable by its odour, is produced.

Wt. per ml : Between 1.04 g and 1.05 g, Appendix 5.19.

Distillation range : None distils below 200° and not less than 94 per cent distils between 202° and 208°, Appendix 5.3.

Refractive index : Between 1.536 and 1.542, Appendix 5.14.

Acid value : Not greater than 0.5, Appendix 3.3.15.

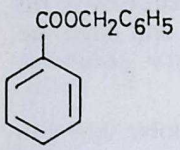
Chlorinated compounds : Mix 2.0 g with 50 ml of *amyl alcohol* in a dry flask, add in small quantities 3 g of *sodium*, connect the flask to a reflux air condenser, warm gently until the evolution of hydrogen ceases, and boil gently for one hour. Cool the liquid to a little below 100° add 50 ml of *water*, 5.0 ml of *0.1N silver nitrate*, and 20 ml of *nitric acid*, and titrate the excess of silver nitrate with *0.1N ammonium thiocyanate*, using *ferric ammonium sulphate solution* as indicator. Repeat the operation without the sample; the difference between the titrations does not exceed 0.3 ml.

Benzaldehyde : Mix in a stoppered cylinder 10 ml with 10 ml of *aldehyde-free alcohol* and 20 ml of *hydroxylamine hydrochloride solution*. Allow to stand for five minutes and titrate with *0.1N sodium hydroxide* to the same green colour as that shown by 20 ml of *hydroxylamine hydrochloride solution* contained in a similar cylinder, both solutions being viewed down the axes of the cylinders; not more than 1.4 ml of *0.1N sodium hydroxide* is required.

Assay : To 1.5 g add 25 ml of a mixture of 1 volume of *acetic anhydride* and 7 volumes of *pyridine* and heat on a water-bath for thirty minutes. Cool, add 25 ml of *water*, and titrate with *N sodium hydroxide*, using *phenolphthalein solution* as indicator. Repeat the operation without benzyl alcohol; the difference between the titrations represents the amount of alkali required by the benzyl alcohol. Each ml of *N sodium hydroxide* is equivalent to 0.1081 g of C_7H_8O.

Storage : Store in tightly-closed containers with minimum space above the level of the liquid.

Benzyl Benzoate



$C_{14}H_{12}O_2$ Mol.Wt. 212.25

Category : Anti-parasitic(scabicide).

Description : Colourless crystals or clear, colourless oily liquid; odour, faintly aromatic; taste, sharp and burning.

Solubility : Practically insoluble in *water*, soluble in *alcohol*, in *chloroform* and in *solvent ether*, insoluble in *glycerin*.

Standards : Benzyl Benzoate is the benzyl ester of benzoic acid. It contains not less than 99.0 per cent and not more than the equivalent of 100.5 per cent w/w of $C_{14}H_{12}O_2$.

Identification : (A) Boil 2 g with 25 ml of *alcoholic potassium hydroxide solution* for two hours in a flask fitted with a reflux condenser. Remove the alcohol on a water-bath, add 50 ml of *water* to the liquid remaining in the flask and distil until the liquid distilling is no longer turbid.

(B) To the liquid remaining in the flask, add *dilute hydrochloric acid* till it is neutral. Divide into two parts; to one part add *ferric chloride test-solution*, a buff-coloured precipitate is produced. To the other part add *hydrochloric acid*; a white crystalline precipitate of benzoic acid is produced.

(C) To the distillate, add 2.5 g of *potassium permanganate*, and 2 ml of *sodium hydroxide solution*, boil for fifteen minutes in a flask fitted with a reflux condenser, cool and filter. To the filtrate add *dilute hydrochloric acid* till it is neutral. Divide into two parts; to one part, add *ferric chloride test-solution*; a buff-coloured precipitate is produced. To the other part add *hydrochloric acid*; a white crystalline precipitate of benzoic acid is produced.

Congealing temperature : Not below 17.0°, Appendix 5.5.

Wt. per ml : Between 1.113 g and 1.118 g, Appendix 5.19.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Refractive index : Between 1.5668 and 1.5670, Appendix 5.14.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Assay : Carry out the method for the *determination of esters*, Appendix 3.3.2, using 40 ml of *0.5N alcoholic potassium hydroxide*. Each ml of *0.5N alcoholic potassium hydroxide* is equivalent to 0.1061 g of $C_{14}H_{12}O_2$.

Storage : Store in well-closed, light-resistant containers.

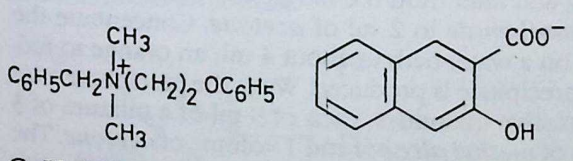
Benzyl Benzoate Application

Category : Anti-parasitic (for the topical treatment of scabies).

Standards : Benzyl Benzoate Application is an emulsion of Benzyl Benzoate in Purified Water containing Emulsifying Wax. It contains not less than 22.5 per cent and not more than 27.5 per cent w/v of $C_{14}H_{12}O_2$.

Assay : Weigh accurately about 8 g and dissolve in 10 ml of *alcohol*, previously neutralised with *0.1 N sodium hydroxide*. Carry out the *determination of esters*, Appendix 3.3.2, using 40 ml of *0.5 N alcoholic potassium hydroxide*. Each ml of *0.5 N alcoholic potassium hydroxide* is equivalent to 0.1061 g of $C_{14}H_{12}O_2$. Calculate the percentage w/v of $C_{14}H_{12}O_2$, from the weight per ml of the sample.

Bephenium Hydroxynaphthoate



$C_{28}H_{29}NO_4$ Mol.Wt. 443.54

Category : Anthelmintic (hookworms).

Dose : 5 g, as a single dose.

Description : Yellow crystalline powder; odourless; taste, bitter.

Solubility : Insoluble in *water*; sparingly soluble in *alcohol*.

Standards : Bephenium Hydroxynaphthoate is *N*-benzyl-*N*,*N*-dimethyl-*N*-(2phenoxyethyl) ammonium-3-hydroxy-2-naphthoate. It contains not less than 99.0 per cent of $C_{28}H_{29}NO_4$, calculated with reference to the dried substance.

Identification : Dissolve 0.2 g in 10 ml of warm *alcohol*, add 15 ml of *picric acid solution* and allow to stand for a few minutes; a precipitate is formed which, after washing with *alcohol* and then with *water*, and drying at 105°, melts at about 134° with decomposition, Appendix 5.11.

Melting range : Between 168° and 173°, with decomposition, Appendix 5.11.

Specific surface area : Not less than 7000 sq cm per g, Appendix 5.17.

Chloride : Boil 2.5 g with 100 ml of *water*, cool in ice and filter. To 20 ml of the filtrate, add 10 ml of *dilute nitric acid*, shake and filter. The filtrate complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphate : To a further 20 ml of the filtrate obtained in the test for **chloride**, add 10 ml of *dilute hydrochloric acid*, shake, and filter; the filtrate complies with the *limit test for sulphates*, Appendix 3.2.8.

Related compounds : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel GF254* as the coating substance, and a mixture of 5 volumes of *butyl alcohol*, 4 volumes of *water* and 1 volume of *acetic acid* as the mobile phase. Apply separately to the plate 5 µl of each of the following solutions in *methyl alcohol* containing (1) 4.0 per cent w/v of the substance being examined; (2) 0.04 per cent w/v of the substance being examined. After removal of the plate allow it to dry in air and examine it under an ultra-violet lamp having a maximum output at about 254 nm. In the chromatograms obtained with solutions (1) and (2), two main spots are revealed, one of which absorbs ultra-violet radiation and the other fluoresces. Any subsidiary absorbing spot in the chromatogram obtained with solution (1) is not greater in intensity than the main absorbing spot revealed in the chromatogram obtained with solution (2).

Spray the plate with *sodium molybdophosphotungstate solution* and then with a 20 per cent w/v solution of *sodium carbonate* and examine the plate immediately. In the chromatogram obtained with solutions (1) and (2), two main spots are revealed one of which is yellowish-blue in colour and the other is greyish-blue in colour and is the faster running of the two. Any subsidiary spot in the chromatogram obtained with the solution (1), other than any subsidiary spot which may have been compared under ultra-violet light, is not greater in intensity than the faster running of the two main spots revealed in the chromatogram obtained with solution (2).

Sulphated ash : Not more than 0.2 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Assay : Weigh accurately about 1.0 g, dissolve in 50 ml of *glacial acetic acid*, add a few drops of *crystal-violet solution* and titrate with *0.1N perchloric acid* to a bluish-green end-point. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.04435 g of $C_{28}H_{29}NO_4$.

Storage : Store in well-closed, light-resistant containers.

Bephenium Hydroxynaphthoate Granules

Category : Anthelmintic (hookworms).

Dose : Bephenium Hydroxynaphthoate, 5 g equivalent to about 2.5 g bephenium base, as a single dose.

Usual strength : The equivalent of 2.5 g of bephenium per single dose.

Description : Yellow granules of irregular particles not exceeding 4 mm in size.

Standards : Bephenium Hydroxynaphthoate Granules contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Bephenium Hydroxynaphthoate, $C_{28}H_{29}NO_4$.

Identification : (A) The granules when examined under screened ultra-violet light exhibit a green fluorescence.

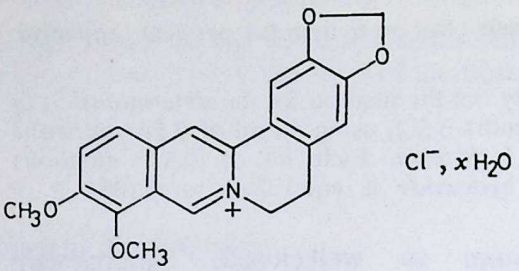
(B) Extract a quantity equivalent to about 0.2 g of Bephenium hydroxynaphthoate with warm *alcohol*, add 15 ml of *picric acid solution* and allow to stand; the precipitate complies with **Identification** test described under Bephenium Hydroxynaphthoate.

Suspension test : Stir 5 g with 50 ml of *water*. The granules are readily wetted to give a uniform suspension.

Assay : Weigh accurately about 1 g of the previously dried material and dissolve in 50 ml of *glacial acetic acid*. Titrate with *0.1N perchloric acid* using *crystal-violet solution* as indicator. Perform a blank titration and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.04435 g of $C_{28}H_{29}NO_4$.

Storage : Store in tightly-closed containers, in a cool place

Berberine Chloride



$C_{20}H_{18}ClNO_4, xH_2O$

Category : Bitter stomachic, anti-bacterial.

Dose : 0.1 g as a single dose.

Description : Pale yellow crystals or crystalline powder; odourless or almost odourless; taste, very bitter.

Solubility : Freely soluble in hot *water*; soluble in hot *alcohol*; sparingly soluble in *methyl alcohol*.

Standards : Berberine Chloride is 5, 6-dihydro-9, 10-dimethoxy-2, 3-methylene-dioxydibenzo [*a, g*] quindizinium chloride hydrate, a quarternary alkaloid present in various species of *Berberis*. It contains not less than 97.0 per cent and not more than the equivalent of 102.0 per cent of $C_{20}H_{18}ClNO_4$, calculated with reference to the anhydrous substance.

Identification : (A) Dissolve 10 mg in 20 ml of *water* by warming, cool and add 1 ml of *potassium iodide solution*; a yellow precipitate is produced.

(B) Dissolve 0.1 g in 20 ml of *water* by warming; add 0.5 ml of *nitric acid*. Cool, set aside for ten minutes and filter. To 3 ml of the filtrate add 1 ml of *silver nitrate solution* and filter. The precipitate dissolves in an excess of *dilute ammonia solution*.

(C) Dissolve 0.4 g in 6 ml of *methyl alcohol* by warming and filter. Add the filtrate to a solution of 0.2 g of *sulphanilamide* in 2 ml of *acetone*. Concentrate the mixture on a water-bath to about 4 ml; an orange to red-brown, precipitate is produced. Wash the precipitate with two successive quantities, each of 5 ml of a mixture of 3 volumes of *methyl alcohol* and 1 volume of *acetone*. The precipitate after drying at 105°, melts at about 220°, with decomposition, Appendix 5.11.

(D) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.001 per cent w/v solution exhibits maxima at 263 nm and 345 nm, Appendix 5.15A.

Clarity of solution : Dissolve 0.1 g in 50 ml of *water* by warming on a water-bath. The resulting solution is clear.

Acidity : Shake 0.1 g with 30 ml of *water* and filter; to the filtrate add two drops of *phenolphthalein solution* and titrate with *0.1N sodium hydroxide* to a red colour, not more than 0.1 ml is required.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Sulphate : Shake 5 g with 2 ml of *dilute hydrochloric acid* and sufficient *water* to produce 50 ml. Filter and discard the first 5 ml of the filtrate. 25 ml of the filtrate complies with the *limit test for sulphates*, Appendix 3.2.8.

Heavy metals : Not more than 30 parts per million, determined on 0.66 g by Method B, Appendix 3.2.4.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Water : Not more than 16.5 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately about 0.2 g and dissolve in 200 ml of *water* by warming. Cool and add sufficient *water* to produce 1000.0 ml. Dilute 10.0 ml with sufficient *water* to produce 100.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 421 nm, Appendix 5.15A. Calculate the content to $C_{20}H_{18}ClNO_4$, from the *extinction* obtained from a solution obtained by dissolving 0.200 g of *potassium dichromate R.S.*, previously dried at 110° for four hours, in a mixture of 50 ml of *water*, and 10 ml of *N sulphuric acid* and sufficient *water* to produce 1000.0 ml and from the following expression :

$$\text{mg of Berberine Chloride } (C_{20}H_{18}ClNO_4) = \frac{c \times a}{B \times 1.006}$$

where :

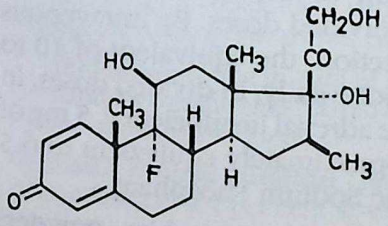
c = concentration in mg of potassium dichromate

a = extinction of the berberine chloride solution

B = extinction of the potassium dichromate solution

Storage : Store in tightly-closed, light-resistant containers.

Betamethasone



$C_{22}H_{29}FO_5$ Mol.Wt. 392.47

Category : Adrenocortical steroid (anti-inflammatory).

Dose : 0.5 to 5 mg daily, in divided doses.

Description : White to creamy-white powder; odourless.

Solubility : Practically insoluble in *water*; sparingly soluble in *alcohol*; very slightly soluble in *chloroform*.

Standards : Betamethasone is 9α-fluoro-11β, 17α, 21-trihydroxy-16β-methylpregna-1, 4-diene-3, 20-dione. It contains not less than 96.0 per cent and not more than the equivalent of 104.0 per cent of $C_{22}H_{29}FO_5$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *betamethasone R.S.*, Appendix 5.15B.

(B) Complies with the test for *identification of steroids*, using *solvent I* and *mobile phase A*, Appendix 3.3.11.

(C) Heat 0.5 ml of *chromic-sulphuric acid* in a test-tube 5 cm long and about 0.6 cm in diameter in a water-bath for five minutes; the solution wets the sides of the tube readily and there is no greasiness. Add 2 or 3 mg of the substance being examined and again heat in a water-bath for five minutes, the solution does not wet the sides of the tube and does not pour easily from the tube.

(D) Place 2 ml of a 0.01 per cent w/v solution in *alcohol* in a stoppered tube, add 10 ml of *phenylhydrazine solution*, mix and place in a water-bath at about 60° for twenty minutes. Cool immediately and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 450 nm, Appendix 5.15A. The E(1 per cent, 1-cm) of the resulting solution at the maximum at about 450 nm is not more than 150.

(E) It melts at about 242° with decomposition, Appendix 5.11.

Specific optical rotation : Between +114° and +122°, determined in a 0.5 per cent w/v solution in *dioxan*, Appendix 5.12.

Light absorption : *Extinction* of a 1-cm layer of a 0.001 per cent w/v solution in *alcohol* at the maximum at about 240 nm, 0.37 to 0.40, Appendix 5.15A. Ratio of the *extinction* at the maximum at about 240 nm to that at 263 nm, 2.0 to 2.1

Related foreign steroids : Complies with the test for *related foreign steroids Method A*, Appendix 3.3.12.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent determined on 1 g by drying "in vacuo at 100°", Appendix 5.8.

Assay : Weigh accurately about 0.1 g and dissolve in sufficient *aldehyde-free ethyl alcohol* to produce 200.0 ml. Dilute 5.0 ml of this solution with *aldehyde-free ethyl alcohol* to 250.0 ml to give the *test solution*. Carry out the *assay of steroids*, Appendix 3.3.10, using *betamethasone R.S.*, for preparing the *standard solution*.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Storage : Store in well-closed, light-resistant containers.

Betamethasone Tablets

Category : Adrenocortical steroid (anti-inflammatory).

Dose : Betamethasone, 0.5 to 5 mg daily, in divided doses.

Usual strengths : 0.5 mg; 1.0 mg.

Standards : Betamethasone Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Betamethasone, $C_{22}H_{29}FO_5$.

Identification : (A) Powder a few tablets and extract with *chloroform*. Evaporate the extract to dryness. The residue complies with **Identification** tests (A), (C) and (D), described under Betamethasone,

(B) The residue obtained in **Identification** test (A) complies with the test for *identification of steroids*, Appendix 3.3.11, using *solvent I* and *mobile phase A*. At a fourth point apply to the plate 2 µl of a mixture of equal volumes of solution (1) and a 0.25 per cent w/v solution of *dexamethasone R.S.* in a mixture of 9 volumes of *chloroform* and 1 volume of *methyl alcohol*. The chromatogram obtained with this solution shows two closely running spots.

Uniformity of content : Powder one tablet, disperse in 10 ml of *water* and extract with three quantities, each of 5 ml, of *chloroform*. Filter the extracts through a plug of cotton wool moistened with *chloroform*. Evaporate the chloroform on a water-bath just to dryness. Cool and dissolve the residue in 50.0 ml of *ethyl alcohol*. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 240 nm, Appendix 5.15A. Calculate the content of $C_{22}H_{29}FO_5$, taking 385 as the value of E(1 per cent, 1-cm) at the maximum at about 240 nm. Repeat the operation with a further nine tablets and calculate the average content of 10 tablets. The content of each tablet is between 90 and 110 per cent of the average except that for one tablet, the content may be between 85 and 115 per cent of the average.

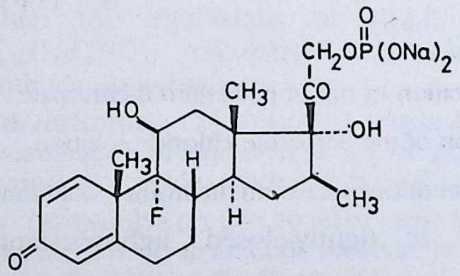
Related foreign steroids : Transfer a quantity of the powdered tablets equivalent to about 3 mg of Betamethasone to a glass-stoppered 50-ml centrifuge tube. Pipette 20 ml of *alcohol* into the tube, shake for two minutes and allow to stand for twenty minutes with occasional shaking. Centrifuge the mixture for five minutes. Pipette 10 ml of the clear supernatant liquid into a glass-stoppered tube and evaporate the *alcohol* on a water-bath with the aid of a current of air to about 0.5 ml, then evaporate without heat to dryness. Pipette 1 ml of a mixture of 9 volumes of *chloroform* and 1 volume of *methyl alcohol*, insert the stopper and mix. Centrifuge, if necessary, to remove any insoluble material. Using this solution as solution (1), carry out the test for *identification of related foreign steroids Method A*, Appendix 3.3.12.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets, weigh accurately a quantity of the powder equivalent to about 2.5 mg of Betamethasone and transfer with the aid of 15 ml of *water* to a separator. Extract with four quantities, each of 25 ml, of *chloroform*, filtering each extract through a plug of cotton wool moistened with *chloroform* into a 250-ml volumetric flask. Add *chloroform* to volume and mix. Transfer 20.0 ml of this solution to a glass-stoppered 50 ml conical flask, evaporate the chloroform on a water-bath just to dryness. Cool and dissolve the residue in 20.0 ml of *aldehyde-free ethyl alcohol* to give the *test solution*. Carry out the *assay of steroids*, Appendix 3.3.10, using *betamethasone R.S.* for preparing the *standard solution*.

Storage : Store in well-closed, light-resistant containers.

Betamethasone Sodium Phosphate



$C_{22}H_{28}FNa_2O_8P$ Mol.Wt. 516.41

Category : Adrenocortical steroid (anti-inflammatory).

Dose : The equivalent of 0.5 to 5 mg of Betamethasone daily, in divided doses. By intravenous or intramuscular injection, the equivalent of 10 to 80 mg of Betamethasone daily, in divided doses, in the treatment of acute adrenal insufficiency. 5 mg of Betamethasone is approximately equivalent to 6.5 mg of Betamethasone Sodium Phosphate.

Description : White or almost white powder; odourless; hygroscopic.

Solubility : Freely soluble in *water*; slightly soluble in *alcohol*; practically insoluble in *chloroform*.

Standards : Betamethasone Sodium Phosphate is disodium 9α-fluoro-11β,17α-dihydroxy-16β-methyl-3, 20-dioxopregna-1,4-dien-21-yl-orthophos-

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

phate. It contains not less than 96.0 per cent and not more than the equivalent of 104.0 per cent of $C_{22}H_{28}FNa_2O_8P$, calculated with reference to the anhydrous substance.

Identification : (A) To 2 ml of a 0.13 per cent w/v solution in *alcohol* in a stoppered tube add 10 ml of *phenylhydrazine solution*, mix, and place in a water-bath at 60° for twenty minutes. Cool immediately; *extinction* of the resulting solution at the maximum at about 450 nm, not more than 0.13, Appendix 5.15A.

(B) Complies with **Identification** test (C) described under Betamethasone.

(C) Heat gently 40 mg with 2 ml of *sulphuric acid* until white fumes are evolved, add *nitric acid* dropwise until oxidation is complete, and cool. Add 2 ml of *water*, heat until white fumes are again evolved, cool, add 10 ml of *water* and neutralise to *litmus paper* with *dilute ammonia solution*. The solution gives the reactions of *sodium*, and of *phosphates*, Appendix 3.1.

(D) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a freshly prepared mixture of 3 volumes of *n-butyl alcohol*, 1 volume of *acetic anhydride*, and 1 volume of *water* as the mobile phase. Apply separately to the plate 2 µl of each of the two solutions in *methyl alcohol* containing (1) 0.25 per cent w/v of the substance being examined and (2) 0.25 per cent w/v of *betamethasone sodium phosphate R.S.* At a third point apply 2 µl of a mixture of equal volumes of solutions (1) and (2) and at a fourth point 2 µl of a mixture of equal volumes of solution (1) and a 0.25 per cent w/v solution of *prednisolone sodium phosphate R.S.* in *methyl alcohol*. After removal of the plate allow it to dry in air until the solvents have evaporated, spray with a 10 per cent v/v solution of *sulphuric acid* in *alcohol*, heat at 120° for ten minutes, allow to cool, and examine under an ultra-violet lamp having a maximum output at 366 nm. The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2); the principal spot in the third chromatogram appears as a single compact spot, and the fourth chromatogram shows two closely running spots.

(E) Dissolve 2 mg in 2 ml of *sulphuric acid* and allow to stand for five minutes; no red colour or yellowish-green fluorescence is produced.

Specific optical rotation : Between +98° and +104°, determined in a 1 per cent w/v solution, Appendix 5.12.

Light absorption : Ratio of the *extinction* of a 1-cm layer of the solution prepared as directed under **Assay** at the maximum at about 241 nm to that at 263 nm, 1.70 to 1.90, Appendix 5.15A.

pH : Between 7.5 and 9.0, determined in a 0.5 per cent w/v solution, Appendix 5.10.

Clarity and colour of solution : A 2.0 per cent w/v solution is clear and colourless.

Inorganic phosphate : Not more than 0.5 per cent, calculated as PO_4 determined by the following method: Weigh accurately about 25 mg dissolved in 10 ml of *water*, add 4 ml of *dilute sulphuric acid*, 1 ml of *ammonium molybdate solution* and 2 ml of *methylaminophenol* with *sulphite solution* and allow to stand for fifteen minutes. Add sufficient *water* to produce 25.0 ml, allow to stand for further fifteen minutes and measure the *extinction* of a 1-cm layer of the resulting solution at 730 nm, Appendix 5.15A. Calculate the content of phosphate from a calibration curve prepared by treating suitable aliquots of a 0.00143 per cent w/v solution of *potassium dihydrogen phosphate* in a similar manner.

Free betamethasone and other derivatives : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using a suitable silica gel as the coating substance and *methyl alcohol* as the mobile phase. Apply separately to the plate 2 µl of each of three solutions in *methyl alcohol* containing (1) 1.0 per cent w/v of the substance being examined, (2) 1.0 per cent w/v of *betamethasone sodium phosphate R.S.* and (3) 0.02 per cent w/v of *betamethasone R.S.* After removal of the plate, allow it to dry in air for five minutes, spray with a 30.0 per cent w/v solution of *zinc chloride* in *methyl alcohol*, heat at about 125° for one hour, and examine under an ultra-violet lamp having a maximum output at about 366 nm. Any spot in the chromatogram obtained with solution (1), other than that corresponding to *betamethasone sodium phosphate R.S.* is not more intense than the spot yielded by *betamethasone R.S.*

Water : Not more than 8.0 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately about 0.2 g and dissolve in sufficient *water* to produce 200.0 ml. Dilute 5.0 ml to 250.0 ml with *water* and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 241 nm, Appendix 5.15A. Calculate the content of $C_{22}H_{28}FNa_2O_8P$, taking 297 as the value of E(1 per cent, 1-cm) at the maximum at about 241 nm.

Storage : Store in tightly-closed, light-resistant containers.

Betamethasone Sodium Phosphate Injection

Category : Adrenocortical steroid (anti-inflammatory).

Dose : In the treatment of acute adrenal insufficiency, by intravenous or intramuscular injection, the equivalent of 10 to 80 mg of Betamethasone daily, in divided doses.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Usual strength : The equivalent of 4 mg of Betamethasone per ml. 5.2 mg of Betamethasone Sodium Phosphate is approximately equivalent to 4 mg of Betamethasone.

Description : Clear, colourless solution.

Standards : Betamethasone Sodium Phosphate Injection is a sterile solution of Betamethasone Sodium Phosphate in Water for Injection. It contains not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Betamethasone, $C_{22}H_{29}FO_5$.

Identification : (A) To a volume equivalent to 4 mg of Betamethasone, add 1 ml of *water* and sufficient *ethyl alcohol* to produce 40 ml. Place 2 ml of this solution in a stoppered tube, add 10 ml of *phenylhydrazine solution*, mix, warm in a water-bath at 60° for twenty minutes, and cool immediately. *Extinction* of 1-cm layer of the resulting solution at the maximum at about 450 nm, not more than 0.1, Appendix 5.15A.

(B) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and, as the mobile phase, a mixture of 3 volumes of *n-butyl alcohol*, 1 volume of *acetic anhydride* and 1 volume of *water*, prepared immediately before use. Apply separately to the plate 5 µl of each of the following four solutions : For solution (1) mix a volume of the injection equivalent to 8 mg of Betamethasone with 20 ml of *water*, 2.5 g of *sodium chloride* and 1 ml of *0.1N hydrochloric acid* and extract with 50 ml of *anaesthetic ether*. Reject the ether layer. Add 0.5 ml of *hydrochloric acid*, extract with 10 ml of *tributyl phosphate*, reject the aqueous layer, and use the organic layer. Solution (2) is prepared in the same manner as solution (1) using 10 mg of *betamethasone sodium phosphate R.S.* instead of the injection. Solution (3) is a mixture of equal volumes of solutions (1) and (2). Solution (4) is a mixture of equal volumes of solution (1) and a solution prepared in the same manner as solution (1) using 10 mg of *prednisolone sodium phosphate R.S.* instead of the injection.

After removal of the plate allow it to dry in air until the odour of solvent is no longer detectable, heat at 110° for ten minutes, spray the hot plate with a 10 per cent v/v solution of *sulphuric acid* in *alcohol*, and again heat at 110° for ten minutes. The chromatograms obtained with solutions (1), (2) and (3), show single spots of similar Rf value; the chromatogram obtained with solution (4) shows two closely running spots.

(C) Evaporate 0.5 ml to dryness on a water-bath; the residue complies with **Identification** test (E) described under Betamethasone Sodium Phosphate.

pH : Between 7.5 and 9.0, Appendix 5.10.

Other requirements : Complies with the requirements stated under Injections.

Assay : Measure accurately a volume equivalent to about 20 mg of Betamethasone and add sufficient *water* to produce 50.0 ml. To 5.0 ml add 20 ml of *water*, and 2 ml of *0.1N hydrochloric acid* and shake with two quantities, each of 25 ml, of *anaesthetic ether*. Wash the ethereal solutions separately with 2, 1, and 1 ml of *water*, add the washings to the acid solution, and discard the ether solutions. To the combined acid solution and washings, add 2 ml of *0.1N sodium hydroxide* and sufficient *water* to produce 200.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 241 nm, Appendix 5.15A, using as the blank, a solution prepared in a similar manner but omitting the injection. Calculate the content of $C_{22}H_{29}FO_5$, taking 391 as the value of E(1 per cent, 1-cm) at the maximum at about 241 nm.

Storage : Store in single-dose or multiple-dose, light-resistant containers in a cool place.

Labelling : The label on the container states the strength in terms of the equivalent amount of Betamethasone in a suitable dose-volume.

Betamethasone Sodium Phosphate Tablets

Category : Adrenocortical steroid (anti-inflammatory).

Dose : The equivalent of 0.5 to 5.0 mg of Betamethasone daily, in divided doses.

Usual strength : The equivalent of 0.5 mg of Betamethasone.

Standards : Betamethasone Sodium Phosphate Tablets contain a quantity of Betamethasone Sodium Phosphate equivalent to not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Betamethasone, $C_{22}H_{29}FO_5$. The tablets may be coloured.

Identification : (A) Comply with **Identification** test (B) described under Betamethasone Sodium Phosphate Injection, using the following four solutions: For solution (1) dissolve a quantity of the powdered tablets equivalent to 2 mg of Betamethasone in 25 ml of *water*, add 2.5 g of *sodium chloride* and 1 ml of *hydrochloric acid*, extract with 25 ml of *chloroform*, and reject the chloroform layer. Extract with 2.5 ml of *tributyl phosphate* and reject the aqueous layer. Solution (2) is prepared in the same manner as solution (1) using 2.5 mg of *betamethasone sodium phosphate R.S.* instead of the powder. Solution (3) is a mixture of equal volumes of solutions (1) and (2). Solution (4) is a mixture of equal volumes of solution (1) and a solution prepared in the same manner as

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

solution (1) using 2.5 mg of *prednisolone sodium phosphate R.S.*, instead of the powder.

(B) Mix a quantity of the powdered tablets equivalent to 0.4 mg of Betamethasone with 1 ml of *sulphuric acid* and allow to stand for five minutes; a pale yellow colour is produced.

Disintegration : The tablets dissolve completely within five minutes, when examined by the *disintegration test for tablets*, Appendix 5.6.1.

Other requirements : Comply with the requirements stated under Tablets.

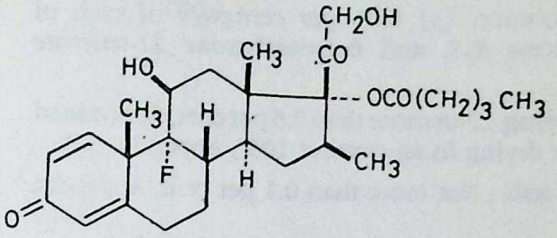
Uniformity of content : Powder one tablet, add 10 ml of *water*, shake vigorously for five minutes and centrifuge. Repeat the extraction with three further quantities, each of 10 ml, of *water*. Combine the extracts and add sufficient *water* to produce 50.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 241 nm, Appendix 5.15A. Calculate the content of $C_{22}H_{29}FO_5$, taking 297 as the value of E(1 per cent, 1-cm) at the maximum at about 241 nm. Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 90 and 110 per cent of the average except that for one tablet the content may be between 85 and 115 per cent of the average.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 10 mg of Betamethasone and dissolve in sufficient *water* to produce 100.0 ml. To 25.0 ml add 2.5 g of *sodium chloride*, dissolve, add 1 ml of *hydrochloric acid*, and shake with three quantities, each of 25 ml, of *chloroform*. Wash each chloroform solution with 1 ml of *0.1N hydrochloric acid*, add the washings to the aqueous solution, and discard the chloroform solution. Extract the aqueous solution with two quantities, each of 10 ml, of *tributyl phosphate* and dilute the combined extracts to 25.0 ml with *methyl alcohol*. To 2.0 ml in a stoppered test-tube add 10.0 ml of *isoniazid solution* and heat at 50° for three hours, protecting the solution from light. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 405 nm, Appendix 5.15A, using as the blank a solution prepared in a similar manner, omitting the powdered tablets. Calculate the content of $C_{22}H_{29}FO_5$ from the *extinction* obtained by repeating the operation using a solution of *betamethasone sodium phosphate R.S.* containing the equivalent of 0.01 per cent w/v of Betamethasone, commencing with the words "To 25.0 ml....", and from the declared content of $C_{22}H_{29}FO_5$ in the *betamethasone sodium phosphate R.S.*

Storage : Store in tightly-closed, light-resistant containers.

Labelling : The label on the container states the strength in terms of the equivalent amount of Betamethasone.

Betamethasone Valerate



$C_{27}H_{37}FO_6$ Mol. Wt. 476.58

Category : Adrenocortical steroid (topical anti-inflammatory).

Description : White to creamy-white powder; odourless.

Solubility : Practically insoluble in *water* and in *light petroleum*; soluble in *alcohol*; freely soluble in *chloroform*.

Standards : Betamethasone Valerate is 9α-fluoro-11β, 17α, 21-trihydroxy-16β-methylpregna-1, 4-diene-3, 20-dione 17-valerate (9α-fluoro-16β-methylprednisolone 17-valerate). It contains not less than 96.0 per cent and not more than the equivalent of 104.0 per cent $C_{27}H_{37}FO_6$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as and have similar relative intensities to, those in the spectrum of *betamethasone valerate R.S.*, Appendix 5.15B.

(B) Complies with the test for *identification of steroids*, Appendix 3.3.11, using *solvent I* and *mobile phase B* and applying to the plate 1 µl of each of the solutions.

(C) Complies with **Identification** test (B) described under Betamethasone.

(D) Carry out **Identification** test (D) described under Betamethasone. The *extinction* of a 1-cm layer of the resulting solution at the maximum at about 450 nm is not more than 0.25.

(E) Heat 50 mg with 2 ml of *0.5N alcoholic potassium hydroxide* in a water-bath for five minutes. Cool, add 2 ml of *sulphuric acid (50 per cent v/v)* and boil gently for one minute; the odour of ethyl valerate is perceptible.

Specific optical rotation : Between +75° and +82°, determined in a 1 per cent w/v solution in *dioxan*, Appendix 5.12.

Light absorption : *Extinction* of a 1-cm layer of a 0.002 per cent w/v solution in *ethyl alcohol* at the maximum at about 240 nm, 0.63 to 0.67, Appendix 5.15 A.

Ratio of the *extinction* at the maximum at about 240 nm to that at 263 nm, 2.1 to 2.3.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Related foreign steroids : Complies with the test for *related foreign steroids, Method B*, Appendix 3.3.12, using for solution (3) 0.03 per cent w/v of each of *betamethasone R.S.* and *betamethasone 21-valerate R.S.*

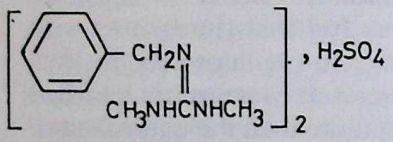
Loss on drying : Not more than 0.5 per cent, determined on 0.5 g by drying in an oven at 105°, Appendix 5.8.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Assay : Carry out the **Assay** described under Betamethasone, using *betamethasone valerate R.S.* for preparing the *standard solution.*

Storage : Store in well-closed, light-resistant containers.

Bethanidine Sulphate



$(C_{10}H_{15}N_3)_2, H_2SO_4$ Mol. Wt. 452.56

Category : Antihypertensive.

Dose : Initial dose, 10 to 20 mg daily, in divided doses; maintenance dose, upto 200 mg daily, in divided doses.

Description : White powder; odourless; taste, bitter.

Solubility : Freely soluble in *water*; soluble in *alcohol*; insoluble in *solvent ether.*

Standards : Bethanidine Sulphate is the sulphate of 2-benzyl-1,3-dimethyl guanidine. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $(C_{10}H_{15}N_3)_2, H_2SO_4$, calculated with reference to the dried substance.

Identification : (A) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.05 per cent w/v solution exhibits three maxima, at 251 nm, 257 nm, and 263 nm; *extinction* at 251 nm, about 0.35, at 257 nm, about 0.45, and at 263 nm, about 0.35, Appendix 5.15A.

(B) Dissolve 25 mg in 5 ml of *water*, add 1.5 ml of *sodium hydroxide solution*, 1 ml of *α-naphthol solution*, and, drop-wise with shaking, 0.5 ml of *dilute sodium hypochlorite solution*; a deep violet colour is produced which darkens on standing.

(C) A solution (1 in 20) gives the reactions of *sulphates*, Appendix 3.2.8.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 25 volumes of *ethyl acetate*, 12 volumes of *glacial acetic acid*, 8 volumes of *water*, and 5 volumes of *alcohol* as the mobile phase. Apply separately to the plate (1) 10 µl of a 5 per cent w/v of the substance being examined in *methyl alcohol.* (2) 2 µl of a 0.05 per cent w/v solution of *methylamine hydrochloride* and (3) 2 µl of a 0.025 per cent w/v solution of *benzylamine sulphate R.S.* After removal of the plate, dry it in a current of air, spray with a 0.5 per cent w/v solution of *ninhydrin* in *isopropyl alcohol*, and heat at 105° for ten to fifteen minutes. The spots in the chromatograms obtained with solutions (2) and (3) are more intense than any corresponding spots in the chromatogram obtained with solution (1).

Apply separately to a second plate (1) 8 µl of a 5 per cent w/v solution of the substance being examined in *methyl alcohol* and (2) 2 µl of a 0.15 per cent w/v solution of *trimethylguanidine sulphate R.S.* in *methyl alcohol.* After removal of the plate, dry it in a current of air, and spray with *dilute potassium iodobismuthate solution.* The spot in the chromatogram obtained with solution (2) is more intense than any corresponding spot in the chromatogram obtained with solution (1).

Sulphated ash : Not more than 0.2 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 1.0 g and dissolve in 50 ml of *glacial acetic acid.* Add ten drops of *crystal-violet solution* and titrate with *0.1N perchloric acid* to bluish-green end-point. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.04526 g of $(C_{10}H_{15}N_3)_2,H_2SO_4$.

Storage : Store in well-closed containers.

Bethanidine Tablets

Category : Antihypertensive.

Dose : Bethanidine Sulphate. Initial dose, 10 to 20 mg daily, in divided doses; maintenance dose, upto 200 mg daily, in divided doses.

Usual strength : 10 mg.

Standards : Bethanidine Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Bethanidine Sulphate, $(C_{10}H_{15}N_3)_2,H_2SO_4$.

Identification : (A) Dissolve a quantity of the powdered tablets equivalent to 0.2 g of Bethanidine Sulphate as completely as possible in 25 ml of *water* and filter. To the filtrate add 2 ml of *dilute sulphuric acid* and 50 ml of

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

picric acid solution. The precipitate after recrystallisation from *water* and drying at 105°, melts at about 148°, Appendix 5.11.

(B) The filtrate obtained in the **Assay** gives the reactions of *sulphates*, Appendix 3.1.

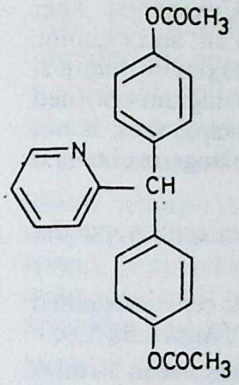
Uniformity of content : Powder one tablet, extract with 5 ml of *water* and centrifuge. Repeat the extraction with two further quantities, each of 5 ml, of *water*. Combine the extracts and add sufficient *water* to produce 20.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 257 nm, Appendix 5.15A. Calculate the content of $(C_{10}H_{15}N_3)_2, H_2SO_4$, taking 9 as the value of E(1 per cent, 1-cm) at the maximum at about 257 nm.

Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 90 and 110 per cent of the average except that for one tablet the content may be between 85 and 115 per cent of the average.

Related substances : Comply with the test described under Bethanidine Sulphate, using as solution (1), a solution prepared in the following manner: Shake a quantity of the powdered tablets equivalent to 50 mg of Bethanidine Sulphate with three quantities, each of 10 ml, of hot *methyl alcohol* and filter; evaporate the combined filtrate to dryness and dissolve the residue in 1.0 ml of *methyl alcohol*.

Assay : Weigh and powder 20 tablets. To a quantity of the powder equivalent to 0.125 g of Bethanidine Sulphate add 50 ml of *water*, and shake for thirty minutes. Add sufficient *water* to produce 100.0 ml, mix and filter. Extract 2.0 ml of the resulting solution with 20.0 ml of *chloroform* and 10 ml of *cobalt thiocyanate reagent*, shake, allow to separate and filter the chloroform layer through a cotton wool plug. Measure the *extinction* of the resulting solution at 625 nm, using *chloroform* in the reference cell, Appendix 5.15A. Calculate the content of $(C_{10}H_{15}N_3)_2, H_2SO_4$, from the *extinction* obtained by repeating the operation using a 0.125 per cent w/v solution of *bethanidine sulphate R.S.* beginning at the words "Extract 2 ml....." and from the declared content of $(C_{10}H_{15}N_3)_2, H_2SO_4$ in the *bethanidine sulphate R.S.*

Bisacodyl



$C_{22}H_{19}NO_4$ Mol. Wt. 361.40

Category : Laxative.

Dose : 5 to 10 mg daily, by mouth.

Description : White or almost white, crystalline powder; odourless; tasteless.

Solubility : Soluble in *chloroform* and in *benzene*; sparingly soluble in *alcohol* and in *methyl alcohol*; slightly soluble in *solvent ether*; practically insoluble in *water*.

Standards : Bisacodyl is 4,4'-(2-pyridylmethylene)-di-(phenylacetate). It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_{22}H_{19}NO_4$, calculated with reference to the dried substance.

Identification : (A) The light absorption, in the range 230 to 350 nm of a 1-cm layer of a 0.001 per cent w/v solution in *0.1N potassium hydroxide* prepared with *methyl alcohol* exhibits a maximum only at 248 nm; *extinction* at 248 nm about 0.65, Appendix 5.15A.

(B) Carry out the method described under **Foreign substances** applying to the plate 5µl each of two solutions in *acetone* containing (1) 0.5 per cent w/v of the substance being examined and (2) 0.5 per cent w/v of *bisacodyl R.S.* The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

Melting range : Between 131° and 135°, Appendix 5.11.

Acidity or Alkalinity : Boil 1.0 g with 20 ml of *carbon dioxide-free water* and cool rapidly. Add two drops of *bromocresol purple solution*; a grey colour is produced or the colour becomes grey on the addition of either 0.05 ml of *0.01N sodium hydroxide* or 0.05 ml of *0.01N hydrochloric acid*.

Foreign substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel GF 254* as the coating substance and a mixture of 1 volume of *xylene* and 1 volume of *ethyl methyl ketone* on the mobile phase. Apply separately to the plate 10 µl of

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

each of two solutions in *acetone* containing (1) 2.0 per cent w/v of the substance being examined and (2) 0.02 per cent w/v of the substance being examined. After removal of the plate, allow it to dry in air, and examine under an ultra-violet lamp having the maximum output at about 254 nm. Any spot in the chromatogram obtained with solution (1), other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (2).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay: Weigh accurately about 0.5 g, dissolve in 50 ml of *glacial acetic acid* and titrate with *0.1 N perchloric acid*, using *1-naphtholbenzein solution* as indicator. Perform a blank determination and make necessary correction. Each ml of *0.1 N perchloric acid* is equivalent to 0.03614 g of $C_{22}H_{19}NO_4$.

Storage : Store in well-closed, light-resistant containers.

Bisacodyl Tablets

Category : Laxative.

Dose : Bisacodyl, 5 to 10 mg daily.

Usual Strength : 5 mg.

Standards : Bisacodyl Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Bisacodyl, $C_{22}H_{19}NO_4$. The tablets are enteric-coated.

Identification : Extract a quantity of the powdered tablets equivalent to 50 mg of Bisacodyl with *chloroform*, filter, evaporate the filtrate to dryness, and dissolve the residue in 10 ml of a 1 per cent w/v solution of *sulphuric acid*, the solution complies with the following tests:

(A) To 2 ml add one drop of *potassium mercuri-iodide solution*; a white precipitate is produced.

(B) To 2 ml add *sulphuric acid*; a reddish-violet colour is produced.

(C) Boil 2 ml with a few drops of *nitric acid*; a yellow colour is produced. Cool and add *sodium hydroxide solution*; the colour becomes yellowish-brown.

Other requirements : Comply with the requirements stated under tablets.

Uniformity of content : Powder one tablet, shake with 70 ml of *chloroform* for thirty minutes, dilute with sufficient *chloroform* to produce 100.0 ml. Mix well, filter and discard the first few ml of the filtrate. Measure the *extinction* of a 1-cm layer of the filtrate at the maximum at about 264 nm, Appendix 5.15A. Calculate the content of $C_{22}H_{19}NO_4$, taking 148 as the value of E(1 per cent, 1-cm) at the maximum at about 264 nm.

Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 90 and 110 per cent of the average except that for the one tablet the content may be between 85 and 115 per cent of the average.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel GF254* as the coating substance and a mixture of 1 volume of *xylene* and 1 volume of *ethyl methyl ketone* as the mobile phase. Apply separately to the plate 10 µl of each of the following solutions: For solution (1) shake a quantity of the powdered tablets equivalent to 20 mg of Bisacodyl with 2 ml of *acetone* for ten minutes, centrifuge, and use the supernatant liquid; for solution (2) dilute 3 volumes of solution (1) to 100 volumes with *acetone*. After removal of the plate, allow it to dry in air, and examine under an ultra-violet lamp having a maximum output at about 254 nm. Any spot in the chromatogram obtained with solution (1), other than the principal spot and any spot having a relative Rf of 1.3 compared with the principal spot (due to tablet excipient), is not more intense than the spot in the chromatogram obtained with solution (2).

Assay : Weigh and powder 20 tablets. Shake a quantity of the powder equivalent to 40 mg of Bisacodyl with 70 ml of *chloroform* for thirty minutes, dilute to 100.0 ml with *chloroform*, mix, filter, and dilute 10.0 ml of the filtrate to 100.0 ml with *chloroform*. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 264 nm, Appendix 5.15A. Calculate the content of $C_{22}H_{19}NO_4$, taking 148 as the value of E(1 per cent, 1-cm) at the maximum at about 264 nm.

Whole Human Blood

Whole Blood (Human)

Category : Blood replenisher.

Description : Deep-red fluid which, on standing, separates into a lower layer of sedimented red cells and a yellow, almost clear, upper layer of plasma, free from visible signs of haemolysis, with a greyish layer between the two consisting of leucocytes and thrombocytes. A layer containing emulsified fat may form on the surface.

Standards : Whole Human Blood is blood drawn from selected human donors and mixed with a suitable anticoagulant.

The donor from whom the blood is drawn must:

(a) be in the age range of 18 to 60 years and be in

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

good health as indicated in part by normal temperature and blood pressure within normal limits,

(b) have blood containing not less than 12.5 per cent w/v of haemoglobin,

(c) as far as can be ascertained after clinical and laboratory examination and the study of his medical history, be free from disease transmissible by blood transfusion,

(d) be free from acute respiratory diseases,

(e) be free from any infectious skin disease at the site of phlebotomy,

(f) have no history of malarial fever within six months of donation,

(g) have no history of viral hepatitis or of close contact with an individual having viral hepatitis within six months of donation and have blood that has given negative results in tests for the presence of hepatitis-B antigen,

(h) have blood that has been tested with negative results for evidence of syphilitic infection.

The frequency of donations of whole blood shall not exceed one every two months, with a maximum volume in any consecutive 12-month period of 2 litres.

The blood is drawn aseptically through a closed system into a suitable sterile container containing a specific amount of Anticoagulant Citrate Dextrose Solution (ACD Solution) or Anticoagulant Citrate Phosphate Dextrose Solution (CPD Solution) which is placed before the container is sterilised. The quantity of anticoagulant solution should not exceed 22 per cent v/v of the final volume of the mixture. The mixture contains not less than 9.7 per cent w/v of haemoglobin, calculated from the haemoglobin content of the donor's blood and the dilution due to the anticoagulant solution.

During the withdrawal of blood the container is gently agitated to ensure thorough mixing. When withdrawal is complete the container is immediately sealed and cooled to 1° to 6°. It is not opened until immediately before transfusion. With every container of blood, a separate sample mixed with the appropriate quantity of anticoagulant solution, is collected for compatibility and other tests.

The volume of blood to be collected in each container shall be determined by the Licencing Authority under the Drugs and Cosmetics Rules, 1945.

Whole Human Blood in containers from which samples have been removed for tests should not be used for transfusion. The following tests are intended for ensuring that the conditions in which the blood is collected and stored are such that if and when tested, the blood will comply with the requirements of the monograph.

Blood group : Determine the blood group (in the sample accompanying each donation) under the ABO system, Appendix 2.39, by examination of both corpuscles and serum, and under the Rh system, Appendix 2.39, by examination of the corpuscles.

Sterility : Complies with the *tests for sterility*, Appendix 4.6.

Haemolysins : Carry out the *test for haemolysins*, Appendix 2.41.

Assay : Determine the haemoglobin content by *photometric haemoglobinometry*, Appendix 2.40.

Storage : Store in the container into which it was originally drawn. The container should be provided with a hermetic, contamination-proof closure. Store at a temperature between 1° and 6° and held constant within 2° range and during transit, between 1° and 10°

Labelling : The label on the container states (1) the ABO group; (2) the Rh group; (3) the total volume of fluid, the proportion of blood, and the nature and volume of anticoagulant solution; (4) the date on which the blood was withdrawn; (5) the expiry date which should not exceed 21 days from the date of withdrawal of blood; (6) the storage conditions; (7) that the blood must not be used for transfusion if there is any visible evidence of haemolysis or other deterioration; (8) for blood of group O whether haemolysins are present or not and if they are, that the blood must be administered only to recipients of blood group O.

Concentrated Human Red Blood Corpuscles

Concentrate of Human Red Blood Cells; Packed Red Cells

Category : Blood replenisher.

Description : Dark red fluid when prepared; after standing, the red corpuscles may form a sediment, leaving a small supernatant layer of yellow plasma.

Standards : Concentrate Human Red Blood

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Corpuscles consist of the red blood cells remaining after separating plasma from human blood. It is prepared from Whole Human Blood, not more than twenty-one days old, preferably not more than fourteen days old and is directly matched with the blood of the intended recipient. It may be prepared by centrifuging or undisturbed sedimentation for the separation of plasma and anticoagulant solution equivalent to not less than 40 per cent of the total volume of Whole Human Blood. A portion of the plasma, sufficient to ensure optimal cell preservation, shall be left. All surfaces that come in contact with the red cells shall be sterile and pyrogen-free and the entire processing of the blood shall be conducted in a sterile system. The final containers used for the Concentrated Human Red Blood Corpuscles shall be the original blood containers unless the method of processing requires a different container. Immediately after processing the containers are stored at a temperature between 1° and 6°.

It contains not less than 15.5 per cent w/v of haemoglobin.

Sterility : The contents of a container, if tested, comply with the *tests for sterility*, Appendix 4.6, but the material from such a container is not used for transfusion.

Assay : Determine the haemoglobin content by *photometric haemoglobinometry*, Appendix 2.40.

Storage : Store in the container which is of colourless and transparent glass, or of a suitable plastic material, is sterile and sealed so as to exclude micro-organisms. Store at temperatures between 1° and 10°, held constant within a range of 2°.

Labelling : The label on the container states (1) the reference number of the Whole Human Blood from which the preparation was made; (2) the ABO and Rh groups of the Whole Human Blood; (3) the date of collection of the Whole Human Blood from which the preparation was made; (4) the storage conditions; (5) the time after which the preparation is not suitable for transfusion; (6) that "the preparation should not be used if there is any evidence of deterioration."

Boric Acid

H_3BO_3 Mol. Wt. 61.83

Category : Local anti-infective.

Description : Colourless plates or white crystals or white crystalline powder, greasy to the touch; odourless; taste, slightly acid and bitter with a sweetish after taste.

Solubility : Soluble in *water* and in *alcohol*; freely soluble in boiling *water*, in boiling *alcohol* and in *glycerin*.

Standards : Boric Acid contains not less than 99.5 per cent and not more than the equivalent of 100.5 per cent of H_3BO_3, calculated with reference to the dried substance.

Identification : (A) Dissolve 0.1 g by gently warming with 5 ml of *methyl alcohol* to which a few drops of *sulphuric acid* have been added. Ignite the solution; the flame has a green border.

(B) Dissolve 3.0 g in 90 ml of boiling *water*, cool; the solution is faintly acid.

Clarity and colour of solution : The solution obtained in **Identification** test (B) is clear or at most very slightly opalescent.

Solubility in alcohol : Dissolve 1.0 g in 10 ml of boiling *alcohol*. The solution is colourless and clear or at most slightly opalescent.

pH : Between 3.8 and 4.8 determined in the solution obtained in **Identification** test (B), Appendix 5.10.

Sulphate : Boil 3 g with 30 ml of *water* and 1 ml of *hydrochloric acid*, cool, and filter; 25 ml of the filtrate complies with the *limit test for sulphates*, Appendix 3.2.8.

Arsenic : Not more than 10 parts per million, Appendix 3.2.1.

Heavy metals : Not more than 20 parts per million, determined by Method A on a solution obtained by dissolving 1.0 g in 2 ml of *dilute acetic acid* and sufficient *water* to produce 25 ml, Appendix 3.2.4.

Loss on drying : Not more than 0.5 per cent, determined on 100 g by drying over *silica gel* for five hours, Appendix 5.8.

Assay : Weigh accurately about 2 g, and dissolve in a mixture of 50 ml of *water* and 100 ml of *glycerin*, previously neutralised to *phenolphthalein solution*. Titrate with *N sodium hydroxide*, using *phenolphthalein solution* as indicator. Each ml of *N sodium hydroxide* is equivalent to 0.06183 g of H_3BO_3.

Storage : Store in well-closed containers.

Labelling : The label on the container states "Not for internal use."

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Busulphan

$CH_3SO_2O(CH_2)_4OSO_2CH_3$

$C_6H_{14}O_6S_2$ Mol. Wt. 246.29

Category : Antineoplastic.

Dose : 2 to 4 mg daily.

Description : White crystalline powder, almost odourless.

Solubility : Slightly soluble in *water* and in *alcohol*; soluble in *acetone*.

Standards : Busulphan is 1,4-Butanediol dimethanesulphonate. It contains not less than 98.0 per cent and not more than the equivalent of 100.5 per cent of $C_6H_{14}O_6S_2$, calculated with reference to the dried substance.

Identification : (A) Fuse 0.1 g with 0.1 g of *potassium nitrate* and 0.25 g of *potassium hydroxide*, cool; dissolve the residue in *water*, acidify with *dilute hydrochloric acid*, and add a few drops of *barium chloride solution*; a white precipitate is produced.

(B) To 0.1 g add 10 ml of *water* and 5 ml of *N sodium hydroxide*. Heat until a clear solution is obtained; an intense, characteristic pyridine-like odour is produced.

(C) Cool the solution in **Identification** test (B) and divide into two equal parts. To one part add 1 drop of *potassium permanganate solution*, the colour changes from purple to violet to blue and finally to emerald-green. Acidify the other part with *dilute sulphuric acid* and add 1 drop of *potassium permanganate solution*; the purple colour is not discharged.

Melting range : Between 115° and 118°, Appendix 5.11.

Acidity : Dissolve 0.20 g in 50 ml of warm *alcohol (70 per cent)* previously neutralised to *methyl red solution*, and titrate with *0.1N sodium hydroxide*, using *methyl red solution* as indicator; not more than 0.05 ml is required.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 2.0 per cent, determined on 0.5 g by drying "in vacuo at 60°", Appendix 5.8.

Assay : Weigh accurately about 0.25 g, add 25 ml of *water* and boil gently under a reflux condenser for thirty minutes. Wash the condenser with a small quantity of *water*, cool and titrate with *0.1N sodium hydroxide*, using *phenolphthalein solution* as indicator. Each ml of *0.1N sodium hydroxide* is equivalent to 0.01232 g of $C_6H_{14}O_6S_2$.

Storage : Store in tightly-closed, light-resistant containers.

CAUTION—Busulphan is very poisonous. Great care should be taken to avoid inhaling the particles of Busulphan and exposing the skin to it.

Busulphan Tablets

Category : Antineoplastic.

Dose : Busulphan, 2 to 4 mg daily; maintenance dose, 0.5 to 2 mg daily.

Usual strength : 2 mg.

Standards : Busulphan Tablets contain not less than 90.0 per cent and not more than 115.0 per cent of Busulphan, $C_6H_{14}O_6S_2$. The tablets are coated.

Identification : Extract a quantity of the powdered tablets equivalent to 50 mg of Busulphan with 20 ml of hot *acetone*, filter, evaporate the acetone, add 15 ml of *water* and 1 ml of *sodium hydroxide solution*, and heat; a characteristic pyridine-like odour is produced.

Disintegration : Maximum time, fifteen minutes, Appendix 5.6.1.

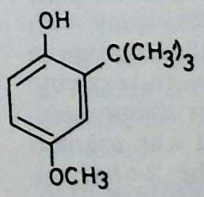
Other requirements : Comply with the requirements stated under Tablets,.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powdered tablets equivalent to 20 mg of Busulphan, extract with 100 ml of hot *acetone*, filter and wash the filter with five quantities, each of 25 ml of *acetone*. Evaporate the combined filtrates to dryness with the aid of a current of air, add to the residue 25 ml of *water*, and boil gently under a reflux condenser for thirty minutes. Wash the condenser with a small quantity of *water*, cool and utrate with *0.01N sodium hydroxide*, using *phenolphthalein solution* as indicator. Each ml of *0.01N sodium hydroxide* is equivalent to 0.001232 g of $C_6H_{14}O_6S_2$.

Storage : Store in well-closed, light-resistant containers.

Butylated Hydroxyanisole

BHA



$C_{11}H_{16}O_2$ Mol. Wt. 180.25

Category : Pharmaceutical aid (anti-oxidant)

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Description : White or almost wnite, crystalline powder or a yellowish white waxy solid; odour, aromatic; taste, slightly bitter with burning sensation.

Solubility : Practically insoluble in *water*; freely soluble in *alcohol*, in *propylene glycol*, in *arachis oil*, and in solutions of the alkali hydroxides.

Standards : Butylated Hydroxyanisole is 2-*t*-butyl-4-methoxyphenol containing a variable amount of 3-*t*-butyl-4-methoxyphenol

Identification : (A) Dissolve, 0.1 g in 10 ml of *alcohol* and add 2 ml of a 2.0 per cent w/v solution of *borax* and a few crystals of *2, 6-dichloroquinone-chlorimide*; a blue colour is produced (distinction from butylated hydroxytoluene)

(B) Dissolve a few crystals in 10 ml of *alcohol*, and add 0.5 ml, of a 0.2 per cent w/v solution of *potassium ferricyanide* and 0.5 ml of a 0.5 per cent w/v solution of *ferric ammonium sulphate* in *N sulphuric acid*; a green to blue colour is produced.

Melting range : Between 62° and 65°, Appendix 5.11.

Hydroquinone : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 4 volumes of *chloroform* and 1 volume of *ethyl acetate* as the mobile phase. Apply separately to the plate 3 µl of each of two solutions in *anaesthetic ether* containing (1) 5.0 per cent w/v of the substance being examined and (2) 0.01 per cent w/v of *hydroquinone*. After removal of the plate, allow it to dry in air for a few minutes, spray with *phosphomolybdic acid solution*. While still damp expose it to the vapour of *strong ammonia solution* and examine immediately, the yellow background has disappeared. The spot in the chromatogram obtained with solution (2) is more intense than any corresponding spot in the chromatogram obtained with solution (1).

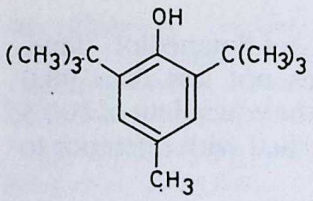
3-*t*-Buty1-4-methoxyphenol : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and *chloroform* as the mobile phase. Apply separately to the plate 2 µl of each of two solutions in *anaesthetic ether* containing (1) 10.0 per cent w/v of the substance being tested and (2) 10.0 per cent w/v of *2-t-butyl-4-methoxyphenol R.S.* and 0.10 per cent w/v of *3-t-butyl-4-methoxyphenol R.S.* applying each solution in four portions. After removal of the plate allow it to dry in air for a few minutes, spray with *phosphomolybdic acid solution*. While still damp expose it to the vapour of *strong ammonia solution*, and examine immediately, the yellow background has disappeared. Any spots in the chromatogram obtained with solution (1) other than that corresponding to the *2-t-butyl-4-methoxyphenol R.S.* are not more intense than the spot shown by the *3-t-butyl-4-methoxyphenol R.S.* in the chromatogram obtained with solution (2).

Sulphated ash : Not more than 0.15 per cent, Appendix 3.2.7

Storage : Store in well-closed, light-resistant containers.

Butylated Hydroxytoluene

BHT



$C_{15}H_{24}O$ Mol. Wt. 220.35

Category : Pharmaceutical aid (anti-oxidant)

Description : Colourless crystals or a white, crystalline powder; odourless; tasteless.

Solubility : Freely soluble in *toluene*; soluble in *acetone*, in *alcohol*, in *benzene*, in *solvent ether*, in *isopropyl alcohol*, in *methyl alcohol*, in *light petroleum*, in fixed oils, and in fats; insoluble in *water*.

Standards : Butylated Hydroxytoluene is 2, 6-di-*t*-butyl-*p*-cresol.

Identification : (A) The light absorption in the range 230 to 350 nm of a 1-cm layer of a 0.005 per cent w/v solution in *ethyl alcohol*, exhibits a maximum only at 278 nm; *extinction* at 278 nm, about 0.43, Appendix 5.15A.

(B) Dissolve 0.1 g in 10 ml of *alcohol*, add 2 ml of a 2.0 per cent w/v solution of *borax* and a few crystals of *2, 6-dichloroquinone-chlorimide*; not more than a faint blue colour is produced (distinction from butylated hydroxyanisole).

(C) Complies with the **Identification** test (B) described under Butylated Hydroxyanisole.

Congealing temperature : Not lower than 69.2°, Appendix 5.5.

Acid value : Not more than 0.05, Appendix 3.3.15.

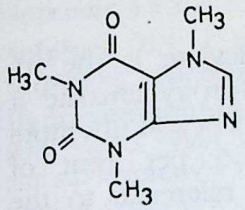
Sulphated ash : Not more than 0.15 per cent, Appendix 3.2.7.

Storage : Store in well-closed containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Caffeine



$C_8H_{10}N_4O_2$ Mol. Wt. 194.19 (anhydrous)

$C_8H_{10}N_4O_2$, H_2O Mol. Wt. 212.21 (hydrated)

Category : Central Nervous System stimulant.

Dose : 0.3 to 0.6 g.

Description : Silky white crystals or white glistening needles or white crystalline powder; odourless; taste, bitter. Sublimes readily.

Solubility : Sparingly soluble in *water* and in *alcohol*; freely soluble in *chloroform*, in boiling *water*; slightly soluble in *solvent ether*.

Standards : Caffeine is 3, 7-dihydro-1, 3, 7-trimethylpurine-2, 6-dione or its monohydrate. It contains not less than 98.5 per cent and not more than the equivalent of 101.0 per cent of $C_8H_{10}N_4O_2$, calculated with reference to the dried substance.

Identification : (A) Take 10 mg in a porcelain dish, add 1 ml of *hydrochloric acid* and 0.1 g of *potassium chlorate*, and evaporate to dryness on a water-bath. Expose the residue to the vapours of *dilute ammonia solution*; a purple colour, which disappears on the addition of a solution of a fixed alkali, is produced.

(B) To a saturated solution add a few drops of *tannic acid solution*; a white precipitate is produced which is soluble in excess of the reagent.

(C) To 5 ml of a saturated solution add 1.5 ml of *0.1N iodine*; the solution remains clear. Add a few drops of *dilute hydrochloric acid*; a brown precipitate is formed. Neutralised with *sodium hydroxide solution*, the precipitate dissolves.

Melting range : Between 235° and 237.5°, determined after drying at 80° for four hours, Appendix 5.11.

Clarity and colour of solution : Dissolve 1.0 g in 50 ml of boiling *water* and cool. The resulting solution is clear and colourless.

Acidity or Alkalinity : Dissolve 0.2 g in 10 ml of boiling *water* and cool. Add two drops of *bromothymol blue solution*. The solution is coloured green or yellow. Titrate with *0.02N sodium hydroxide* to a blue colour. Not more than 0.1 ml is required.

Alkaloids : To 1.0 g add 10 ml of *water* and 2 ml of *dilute sulphuric acid*. Shake vigorously, cool in ice water, filter and to the filtrate add ten drops of *potassium mercuric-iodide solution*; the solution remains clear for not less than five minutes.

Arsenic : Not more than 3 parts per million, Appendix 3.2.1.

Heavy metals : Not more than 20 parts per million, determined by Method A, Appendix 3.2.4, on the following solution: Mix 2.0 g with 5 ml of *0.1N hydrochloric acid* and 45 ml of *water*, warm gently until solution is complete, and cool to room temperature. Use 25 ml of the resulting solution.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent (for the anhydrous form) and 8.5 per cent (for the monohydrate), determined on 1.0 g by drying in an oven at 80° for four hours, Appendix 5.8.

Assay : Weigh accurately about 0.4 g of the sample, finely powdered and dissolve with warming in 40 ml of *acetic anhydride*. Cool, add 80 ml of *benzene* and titrate with *0.1N perchloric acid*, determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.01942 g of $C_8H_{10}N_4O_2$.

Storage : Store in tightly-closed containers.

Labelling : The label on the container states whether it is anhydrous or monohydrate.

Calamine

Category : Topical protectant.

Description : Fine, amorphous pink or reddish-brown powder; odourless; practically tasteless.

Solubility : Insoluble in *water*; practically completely soluble in mineral acids.

Standards : Calamine is zinc oxide with a small proportion of ferric oxide. It contains not less than 98.0 per cent and not more than the equivalent of 100.5 per cent of ZnO, calculated with reference to the ignited substance.

Identification : (A) Shake 1 g with 10 ml of *dilute hydrochloric acid* and filter; the filtrate gives the reactions of *zinc*, Appendix 3.1.

(B) To 1 g add 10 ml of *dilute hydrochloric acid*, heat to boiling and filter; to the filtrate add a few drops of *ammonium thiocyanate solution*; a reddish colour is produced.

Acid-insoluble substances : Dissolve 1 g in 25 ml of warm *dilute hydrochloric acid*. If any insoluble residue remains, collect it on a tarred filter. Wash with *water*, dry

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

to constant weight at 105°, cool and weigh; the weight does not exceed 20 mg.

Alkaline substances : Digest 1 g with 20 ml of warm *water*, filter, add two drops of *phenolphthalein solution*; if a red colour is produced not more than 0.2 ml of *0.1N sulphuric acid* is required to discharge it.

Arsenic : Not more than 8 parts per million, Appendix 3.2.1.

Calcium : Dissolve 0.5 g in a mixture of 10 ml of *water* and 2.5 ml of *glacial acetic acid*, and warm on a water-bath until dissolved. Filter to 0.5 ml of the filtrate, add 15 ml of *5N ammonia* and 2 ml of a 2.5 per cent w/v solution of *ammonium oxalate*, and allow to stand for two minutes; the solution remains clear.

Lead : Dissolve 2.0 g in a mixture of 20 ml of *water* and 5 ml of *glacial acetic acid*, filter, and add 0.25 ml of *potassium chromate solution*; the solution remains clear for five minutes.

Water-soluble dyes : Shake 1.0 g with 10 ml of *water* and filter; the filtrate is colourless.

Alcohol-soluble dyes : Shake 1.0 g with 10 ml of *alcohol (90 per cent)* and filter; the filtrate is colourless.

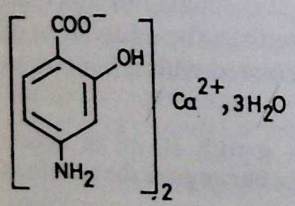
Loss on ignition : Not more than 2.0 per cent, determined on 2.0 g by igniting to constant weight at a temperature not lower than 900°.

Assay : Weigh accurately about 1.5 g and digest with 50.0 ml of *N sulphuric acid*, applying gentle heat until no further solution occurs. Filter and wash the residue with hot *water* until the last washing is neutral to *litmus paper*. To the combined filtrate and washings, add 2.5 g of *ammonium chloride*, cool, and titrate with *N sodium hydroxide* using *methyl orange solution* as indicator. Each ml of *N sulphuric acid* is equivalent to 0.04068 g of ZnO.

Storage : Store in well-closed containers.

Calcium Aminosalicylate

Calcium PAS



$C_{14}H_{12}CaN_2O_6, 3H_2O$ Mol. Wt. 398.38

Category : Antibacterial (tuberculostatic).

Dose : 10 to 20 g daily, in divided doses.

Description : White or slightly yellow crystalline powder; odourless; taste, salty and unpleasant; hygroscopic.

Solubility : Freely soluble in *water*; slightly soluble in *alcohol*; practically insoluble in chloroform and in *solvent ether*.

Standards : Calcium Aminosalicylate is the trihydrate of calcium 4-amino-2-hydroxybenzoate. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_{14}H_{12}CaN_2O_6$, calculated with reference to the anhydrous substance.

Identification : (A) Dissolve 5 mg in *water* and add a few drops of *ferric chloride test-solution*; a purple-red colour is produced; add *acetic acid* or *alcohol*; the purple-red colour persists.

(B) Dissolve 10 mg in 5 ml of *water*, add 0.5 ml of *dilute hydrochloric acid*, 1 drop of a 1.0 per cent w/v solution of *sodium nitrite* and 5 drops of a 1.0 per cent w/v solution of *α-naphthylamine* in *alcohol*; a red colour is produced; add *sodium hydroxide solution* till alkaline; the red colour changes to orange.

(C) A solution (1 in 20) gives the reactions of *calcium*, Appendix 3.1.

Clarity of solution : A 2.0 per cent w/v solution is not more turbid than a solution produced by adding 0.1 ml of *0.02N hydrochloric acid* to a mixture of 48 ml of *water*, 1 ml of *nitric acid* and 1 ml of *silver nitrate solution*.

pH : Between 6.0 and 8.0, determined in a 2.0 per cent w/v solution, Appendix 5.10.

3-Aminophenol : Not more than 0.2 per cent, determined by the following method: Weigh accurately an amount, calculated on the basis of the **Assay**, of Calcium Aminosalicylate, equivalent to 0.562 g of anhydrous calcium aminosalicylate, add 1.8 ml of *N sodium hydroxide* and dilute to 80 ml with *water*. Add 10 ml of *dilute sulphuric acid* and dilute to 100.0 ml with *water* and mix. Within ten minutes of the addition of the acid transfer 5.0 ml of the solution to a 100 ml graduated flask immersed in an ice-bath and containing 50 ml of *water* at 5° add 2.5 ml of a 1.0 per cent w/v solution of *sodium nitrite*. Mix and allow to stand in the ice-bath for exactly three minutes. Add 25 ml of *sodium carbonate solution*, mix and place the flask in a water-bath at 25° for fifteen minutes. Dilute to volume with *water* and allow to stand at 25° for three hours. Measure the *extinction* (A) of a 1-cm layer of the resulting solution at the maximum at about 430 nm, Appendix 5.15A. Calculate the percentage of 3-aminophenol in the sample from the formula.

$$\left(\frac{A-0.32}{1.09}\right)$$

5-Aminosalicylic acid : Dissolve 0.5 g in 5 ml of *water*, add 0.002 g of *resorcinol* and 2 drops of *iodine solution*; no purple colour is produced.

Chloride : Dissolve 0.9 g in 10 ml of *water* and add 3 ml of *acetic acid*, filter, wash the residue with five successive quantities each of 5 ml of *water*, mix the filtrate and

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

washings and dilute to 50 ml with *water*; 10 ml of the solution complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphate : 0.5 g complies with the *limit test for sulphates*, Appendix 3.2.8.

Hydrogen sulphide and sulphur dioxide : Shake 1 g with 5 ml of *water*, add 5 ml of *dilute hydrochloric acid* and stir vigorously. No odour of hydrogen sulphide or of sulphur dioxide is detectable and the vapour does not darken moistened *lead acetate paper*.

Arsenic : Not more than 2 parts per million, Appendix 3.2.1.

Heavy matals : Not more than 20 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

Calcium : Between 11.3 per cent and 11.8 per cent, determined by the following method: Weigh accurately about 0.8 g and dissolve in 50 ml of *water*. Titrate with *0.05M disodium ethylenediamine tetraacetate* to within a few ml of the expected end-point. Add 8 ml of *sodium hydroxide solution*, 0.1 g of *calcon mixture* and continue the titration until the colour of the solution changes from pink to a full blue colour. Each ml of *0.05M disodium ethylenediamine tetraacetate* is equivalent to 0.002004 g of Ca.

Water : Not more than 14.0 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately about 0.5 g and dissolve in 75 ml of *water*; add 10 ml of *hydrochloric acid*, 1 g of *potassium bromide* and cool to 15° and carry out the *nitrite titration*, Appendix 3.3.4.

Each ml of *0.1M sodium nitrite* is equivalent to 0.01722 g of $C_{14}H_{12}CaN_2O_6$.

Storage : Store in tightly-closed, light-resistant containers.

Calcium Aminosalicylate Tablets

Calcium PAS Tablets

Category : Antibacterial (tuberculostatic).

Dose : Calcium aminosalicylate, 10 to 20 g daily, in divided doses.

Usual strength : 0.5 g.

Standards : Calcium Aminosalicylate Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Calcium Aminosalicylate, $C_{14}H_{12}CaN_2O_6, 3H_2O$. The tablets may be coated.

Identification : (A) Digest a quantity of the powdered tablets equivalent to about 3 g of Calcium Aminosalicylate, with 50 ml of *water*, and filter. To the filtrate add 15 ml of *dilute acetic acid* and filter and set aside for precipitation. Collect the precipitate on a filter paper, wash well with *water* and dry at 105° for thirty minutes; the residue complies with **Identification** tests (A) and (B) described under Calcium Aminosalicylate.

(B) The powdered tablets give the reactions of *calcium*, Appendix 3.1.

3-Aminophenol : Not more than 0.77 per cent, determined by the following method: Weigh accurately a quantity of the powdered tablets equivalent to 1.30 g of anhydrous calcium aminosalicylate (calculated on the basis of the **Assay** of the powdered tablets), transfer to a 100 ml graduated flask and dissolve the soluble portion in about 50 ml of *water*. Dilute to volume with *water*, mix and filter, discarding the first 15 ml of the filtrate. Transfer 50.0 ml of the subsequent filtrate to a 100-ml graduated flask and proceed as directed in the test for *3-aminophenol* under Calcium Aminosalicylate, beginning at the words "dilute to 80 ml with *water*.....".

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 0.4 g of Calcium Aminosalicylate, add 25 ml of *water* and shake frequently for ten minutes or until all the calcium aminosalicylate is dissolved. Add 10 ml of *hydrochloric acid*, 1 g of *potassium bromide* and 50 ml of *water*. Cool to 15° and carry out the *nitrite titration*, Appendix 3.3.4. Each ml of *0.1M sodium nitrite* is equivalent to 0.019920 g of $C_{14}H_{12}CaN_2O_6, 3H_2O$.

Storage : Store in tightly-closed, light-resistant containers.

Calcium Carbonate

Precipitated Chalk

$CaCO_3$ Mol. Wt. 100.09

Category : Antacid.

Dose : 1 to 5 g.

Description : Fine, white, microcrystalline powder; odourless; tasteless.

Solubility : Practically insoluble in *water* and in *alcohol*; slightly soluble in *water* containing carbon dioxide, or any ammonium salt. Dissolves with effervescence in *dilute acetic acid* and in *dilute hydrochloric acid* and in *dilute nitric acid*.

Standards : Calcium Carbonate is precipitated Calcium Carbonate. It contains not less than 98.0 per cent and not more than the equivalent of 100.5

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

per cent of $CaCO_3$, calculated with reference to the dried substances.

Identification : To a few mg add *acetic acid*; effervescence is produced and the resulting solution, after boiling, gives the reactions of *calcium*, Appendix 3.1.

Acid-insoluble substances : Not more than 0.2 per cent, determined by the following method: Mix 5.0 g with 10 ml of *water* and add *hydrochloric acid*, dropwise, with shaking until effervescence ceases. Boil for two minutes, allow to cool, dilute to about 200 ml and filter through a sintered-glass filter. Wash the residue with four quantities, each of 5 ml of hot *water* and dry the residue at 105° for one hour.

Magnesium and alkali metals : Not more than 1.0 per cent, determined by the following method: Dissolve 1.0 g in 10 ml of *dilute hydrochloric acid*, neutralise the solution by adding *dilute ammonia solution*, add 2 ml of *acetic acid*, heat the solution to boiling and add 50 ml of hot *ammonium oxalate solution*. Cool, dilute to 100 ml with *water* and filter. To 50 ml of the filtrate add 1.5 ml of *dilute sulphuric acid*, evaporate to dryness on a water-bath, heat the residue to redness, allow to cool and weigh.

Soluble alkali : Boil 5 g with 100 ml of *water* for five minutes, filter immediately and cool. The filtrate requires for neutralisation not more than 2.5 ml of *0.1 N sulphuric acid* using *methyl orange solution* as indicator.

Barium : Dissolve 0.6 g in 10 ml of *dilute acetic acid* by boiling, cool and add 10 ml of *calcium sulphate solution*. The solution remains clear for not less than fifteen minutes.

Iron : Dissolve 0.2 g in 5 ml *water* and 0.5 ml of *iron-free hydrochloric acid*, boil and dilute to 40 ml with *water*, the solution complies with the *limit test for iron*, Appendix 3.2.5.

Arsenic : Not more than 4 parts per million, Appendix 3.2.1.

Heavy metals : Not more than 20 parts per million, determined by Method A, Appendix 3.2.4, on a solution prepared by the following method: To 1 g add 5 ml of *water*, and slowly add 8 ml of *dilute hydrochloric acid*, shake, and evaporate to dryness on a water-bath. Dissolve the residue in 20 ml of *water*, filter, add to the filtrate 3 ml of *dilute acetic acid* and *water* to make 25 ml.

Chloride : 1 g dissolved in *water* by the addition of 3 ml of *nitric acid* complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphate : Suspend 0.5 g in 5 ml of *water* and add dropwise sufficient *dilute hydrochloric acid* to effect solution. Add 2 ml of *dilute hydrochloric acid*; the resultant solution complies with the *limit test for sulphates*, Appendix 3.2.8.

Loss on drying : Not more than 2.0 per cent, determined on 1.0 g by drying in an oven at 200°, Appendix 5.8.

Assay : Weigh accurately about 0.1 g and dissolve in 3 ml of *dilute hydrochloric acid* and 10 ml of *water*. Boil for ten minutes, cool, dilute to 50 ml with *water*. Titrate with *0.05 M disodium ethylenediamine tetraacetate* to within a few ml of the expected end-point, add 8 ml of *sodium hydroxide solution* and 0.1 g of *calcon mixture* and continue the titration until the colour of the solution changes from pink to a full blue colour. Each ml of *0.05 M disodium ethylenediamine tetraacetate* is equivalent to 0.005004 g of $CaCO_3$.

Storage : Store in well-closed containers.

Calcium Chloride

Calcium Chloride Dihydrate

$CaCl_2, 2H_2O$ Mol. Wt. 147.02

Category : Calcium replenisher.

Dose : 1 to 2 g, by mouth; 5 to 10 ml of a 10 per cent solution by slow intravenous injection.

Description : White, crystalline powder; or fragments or granules; odourless; hygroscopic.

Solubility : Freely soluble in *water*, in *alcohol*, and in boiling *alcohol*; very soluble in boiling *water*.

Standards : Calcium Chloride contains not less than 97.0 per cent and not more than the equivalent of 103.0 per cent of $CaCl_2, 2H_2O$.

Identification : A solution (1 in 10) gives the reactions of *calcium*, and of *chlorides*, Appendix 3.1.

Clarity and colour of solution : A 10.0 per cent w/v solution is clear and colourless.

Acidity or Alkalinity : To 10 ml of a freshly prepared 10.0 per cent w/v solution add two drops of *phenolphthalein solution*. Titrate with *0.01 N hydrochloric acid* or *0.01 N sodium hydroxide*; not more than 0.2 ml is required.

Arsenic : Not more than 3 parts per million, Appendix 3.2.1.

Heavy metals : Not more than 10 parts per million, determined by Method A, Appendix 3.2.4, on a solution of 2.0 g in 25 ml of *water*.

Aluminium and phosphate : To 10 ml of a 5.0 per cent w/v solution, add two drops of *dilute hydrochloric acid* and one drop of *phenolphthalein solution*. Add *ammonium chloride-ammonium hydroxide solution* dropwise, until the solution is faintly pink, add the drops in excess, and heat the liquid to boiling, no turbidity or precipitate is produced.

Magnesium and alkali salts : Not more than 1.0 per cent, determined by the following method: Dissolve 1 g in

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

50 ml of *water*, add 0.5 g of *ammonium chloride* and proceed as described under Calcium Carbonate, beginning at the words "heat the solution to boiling....."

Iron : Dissolve 0.3 g in 0.5 ml of *hydrochloric acid* and 25 ml of *water*; the resulting solution complies with the *limit test for iron*, Appendix 3.2.5.

Assay : Weigh accurately about 0.15 g and dissolve in 50 ml of *water*. Carry out the **Assay** described under Calcium Carbonate beginning at the words "Titrate with.....". Each ml of *0.05M disodium ethylenediamine tetraacetate* is equivalent to 0.007351 g of $CaCl_2, 2H_2O$.

Storage : Store in tightly-closed containers.

Calcium Gluconate

$C_{12}H_{22}CaO_{14}, H_2O$ Mol. Wt. 448.40

Category : Calcium replenisher.

Dose : By intramuscular or intravenous injection, 1 to 2 g; oral, 1 to 5 g.

Description : White, crystalline powder or granules; odourless; almost tasteless.

Solubility : Sparingly (and slowly) soluble in *water*; freely soluble in boiling *water*; insoluble in *alcohol*.

Standards : Calcium Gluconate contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of $C_{12}H_{22}CaO_{14}, H_2O$.

Identification : (A) To 1 ml of a 3 per cent w/v solution, add 1 drop of *ferric chloride test-solution*; a yellow colour is produced.

(B) To 0.75 g in 7.5 ml of warm *water*, add 1 ml of *glacial acetic acid* and 1.5 ml of freshly distilled *phenylhydrazine*. Heat the mixture on a water-bath for thirty minutes and allow to cool. Scratch the inner surface of the tube with a glass rod until crystals of gluconic acid phenylhydrazide begin to form. Set aside for ten minutes, filter, dissolve the precipitate in 10 ml of hot *water*, add a small amount of *decolourising charcoal*, and filter in a test-tube. Allow the filtrate to cool and scratch the inner surface of the tube; white crystals are obtained, which melt at about 200°, with decomposition.

(C) A solution (1 in 10) gives the reactions of *calcium*, Appendix 3.1.

Clarity and colour of solution : Dissolve 2.0 g in *water* at a temperature below 60° and dilute to 100 ml with *water*. The solution is clear at 60° and is colourless. When cooled to room temperature it may become very slightly opalescent.

Acidity or Alkalinity : Dissolve 0.5 g in 20 ml of *water*, add 0.1 ml of *0.01N hydrochloric acid* and 0.1 ml of *phenolphthalein solution*; no colour is produced. Add 0.3 ml of *0.01N sodium hydroxide*; a pink colour is produced.

Arsenic : Not more than 2 parts per million, Appendix 3.2.1.

Heavy metals : Not more than 20 parts per million, determined by Method A on 1.0 g dissolved in 4 ml of *dilute hydrochloric acid* and sufficient *water* to produce 25 ml, Appendix 3.2.4.

Chloride : 0.5 g complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphate : 2 g complies with the *limit test for sulphates*, Appendix 3.2.8.

Sucrose and reducing sugars : To 10 ml of a 5 per cent w/v solution in hot *water*, add 2 ml of *dilute hydrochloric acid*, and boil for about two minutes. Cool, add 15 ml of *sodium carbonate solution*, allow to stand for five minutes, and filter. Add 5 ml of the clear filtrate to 2 ml of *potassium cupri-tartrate solution* and boil for two minutes; no red precipitate is formed.

Assay : Weigh accurately about 0.5 g and dissolve in 50 ml of warm *water*; cool, add 5.0 ml of *0.05M magnesium sulphate* and 10 ml of *strong ammonia-ammonium chloride solution* and titrate with *0.05M disodium ethylenediamine tetraacetate*, using *mordant black II mixture* as indicator. From the volume of *0.05M disodium ethylenediamine tetraacetate* required, subtract the volume of *0.05M magnesium sulphate* added. Each ml of the remainder is equivalent to 0.022420 g of $C_{12}H_{22}CaO_{14}, H_2O$.

Storage : Store in well-closed containers.

Calcium Gluconate Injection

Category : Calcium replenisher.

Dose : Calcium Gluconate, by intramuscular or intravenous injection, 1 to 2 g.

Usual strength : 1 g in 10 ml.

Standards : Calcium Gluconate Injection is a sterile solution of Calcium Gluconate in Water for Injection. Not more than 5.0 per cent of the Calcium Gluconate may be replaced with suitable calcium salts as stabiliser. It contains a quantity of calcium equivalent to not less than 8.5 per cent and not more than 9.4 per cent of the stated content of Calcium Gluconate.

Identification : (A) It gives the reactions of *calcium*, Appendix 3.1.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

(B) To 1 ml add one drop of *ferric chloride test-solution*; an intense yellow colour is produced.

(C) 5 ml complies with **Identification** test (B) described under Calcium Gluconate.

pH : Between 6.0 and 8.2, Appendix 5.10.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using a quantity containing the equivalent of not less than 0.2 g of Calcium Gluconate per kg of the rabbit's weight.

Other requirements : Complies with the requirements stated under Injections.

Assay : To a volume equivalent to 0.5 g of Calcium Gluconate, add 50 ml of *water* and complete the **Assay** described under Calcium Gluconate, beginning at the words "add 5.0 ml of *0.05M magnesium sulphate*.....". Each ml of the remainder is equivalent to 0.002004 g of Ca.

Storage : Calcium Gluconate Injection is a super-saturated solution and must be completely free from solid particles.

Labelling : The label on the container states (1) the strength as the percentage w/v of Calcium Gluconate equivalent to the total amount of calcium present; (2) that solutions containing visible solid particles must not be used. The label on the container or the label on the package also states the percentage of any added stabilising agent.

Calcium Gluconate Tablets

Category : Calcium replenisher.

Dose : Calcium Gluconate, 1 to 4 g.

Usual strengths : 0.325 g, 0.5 g, 0.65 g and 1 g.

Standards : Calcium Gluconate Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Calcium Gluconate $C_{12}H_{22}O_{14}Ca, H_2O$.

Identification : A warm filtered solution of the tablets, equivalent to a 10 per cent w/v solution of Calcium Gluconate complies with the **Identification** tests, described under Calcium Gluconate.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 0.5 g of Calcium Gluconate and ignite, gently at first, until free from carbon. Cool, add 10 ml of *water* and sufficient *dilute hydrochloric acid*, dropwise, to effect complete solution of the residue. Neutralise with *dilute ammonia solution*, and complete the **Assay** described under Calcium Gluconate, beginning at the words "add 5.0 ml of *0.05M magnesium sulphate*.....". Each ml of the remainder is equivalent to 0.022420 g of $C_{12}H_{22}O_{14}Ca, H_2O$.

Storage : Store in well-closed containers.

Calcium Hydroxide

$Ca(OH)_2$ Mol. Wt. 74.09

Category : Astringent.

Description : Soft, white powder; taste, alkaline and slightly bitter.

Solubility : Slightly soluble in *water*; soluble in *glycerin* and in aqueous solutions of sugars; insoluble in *alcohol*.

Standards : Calcium Hydroxide contains not less than 90.0 per cent of $Ca(OH)_2$.

Identification : A solution in *acetic acid* gives the reactions of *calcium*, Appendix 3.1.

Alkalinity : A solution is alkaline to *phenolphthalein solution*.

Arsenic : Not more than 4 parts per million, Appendix 3.2.1.

Heavy metals : Not more than 40 parts per million, determined by Method A, Appendix 3.2.4, on the solution obtained in the following manner: Dissolve 1 g in 10 ml of *dilute hydrochloric acid* and evaporate on a water-bath to dryness. Dissolve the residue in 20 ml of *water*, and filter. Dilute the filtrate with *water* to 40 ml, and to 20 ml of the resulting solution add 0.1 ml of *dilute hydrochloric acid* and sufficient *water* to produce 25 ml.

Aluminium, iron, phosphate and acid-insoluble matter : Dissolve 2.0 g in a mixture of 10 ml of *hydrochloric acid* and 75 ml of *water*, boil to remove carbon dioxide, and make alkaline with *dilute ammonia solution*, using *methyl red solution* as indicator. Boil for one minute, filter, and wash the precipitate with a hot 2 per cent w/v solution of *ammonium chloride*. Dissolve the precipitate as completely as possible by passing 20 ml of hot *dilute hydrochloric acid* through the filter, and wash the filter with sufficient hot *water* to adjust the volume of the solution to 50 ml. Boil the solution and make alkaline with *dilute ammonia solution*, using *methyl red solution* as indicator. Boil for one minute, filter through the same filter, wash the precipitate with a hot 2 per cent w/v solution of *ammonium nitrate*, dry, and ignite at a temperature not lower than 1000°; the residue weighs not more than 20 mg.

Chloride : 1.0 g, dissolved in *water* with the addition of 4 ml of *nitric acid*, complies with the *limit test for chlorides*, Appendix 3.2.2.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Sulphate : 0.15 g, dissolved in *water* with the addition of 3.5 ml of *dilute hydrochloric acid*, complies with the *limit test for sulphates*, Appendix 3.2.8.

Assay : Weigh accurately about 3 g and shake gently in a 1000-ml flask with 10 ml of *alcohol*, previously neutralised to *phenolphthalein solution*. Add 490 ml of a 10 per cent w/v solution of *sucrose*, previously neutralised to *phenolphthalein solution*, shake vigorously for five minutes, and then at frequent intervals during four hours. Filter off 250 ml, and titrate with *N hydrochloric acid*, using *phenolphthalein solution* as indicator. Each ml of *N hydrochloric acid* is equivalent to 0.03705 g of $Ca(OH)_2$.

Storage : Store in tightly-closed containers.

Calcium Lactate

$C_6H_{10}CaO_6, xH_2O$ Mol. Wt. 218.22 (anhydrous)

Category : Calcium replenisher.

Dose : 1 to 5 g.

Description : White granules or powder; odourless or odour, slight and not unpleasant. The pentahydrate is somewhat efflorescent.

Solubility : Soluble in *water*; readily soluble in hot *water*.

Standards : Calcium Lactate is the hydrated calcium salt of 2-hydroxy propionic acid. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_6H_{10}CaO_6$, calculated with reference to the anhydrous substance.

Identification : (A) A solution (1 in 20) gives the reactions of *calcium*, Appendix 3.1.

(B) A solution acidified with *sulphuric acid* and warmed with *potassium permanganate* develops the odour of acetaldehyde.

Acidity or Alkalinity : To 10 ml of a 5.0 per cent w/v solution add 0.1 ml of *0.01N hydrochloric acid* and 2 drops of *phenolphthalein solution*; no colour is developed; add 0.6 ml of *0.01N sodium hydroxide*; a pink colour is produced.

Arsenic : Not more than 2 parts per million, Appendix 3.2.1.

Iron : 0.5 g complies with the *limit test for iron*, Appendix 3.2.5.

Heavy metals : Not more than 20 parts per million, determined by Method A on 1.0 g dissolved in 2.5 ml of *dilute hydrochloric acid* and sufficient *water* to produce 25 ml, Appendix 3.2.4.

Chloride : Dissolve 0.5 g in *water* by the addition of 2 ml of *nitric acid*; the solution complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphate : Dissolve 1 g in *water* by the addition of 2 ml of *hydrochloric acid*; the solution complies with the *limit test for sulphates*, Appendix 3.2.8.

Reducing sugars : Dissolve 1 g in 10 ml of *water*, add 5 ml of *potassium cupri-tartrate solution* and boil; not more than a slight brick-red precipitate is produced.

Water : Not more than 30.0 per cent, determined on 1 g by drying in an oven at 120° for four hours, Appendix 3.3.25.

Assay : Weigh accurately about 0.3 g, dissolve in 50 ml of *water* and complete the **Assay** described under Calcium Gluconate, beginning at the words "add 5.0 ml of *0.05M magnesium sulphate*....". Each ml of the remainder is equivalent to 0.01091 g of $C_6H_{10}CaO_6$.

Storage : Store in tightly-closed containers.

Calcium Lactate Tablets

Category : Calcium replenisher.

Dose : Calcium Lactate, 1 to 5 g.

Usual strength : 0.3 g.

Standards : Calcium Lactate Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Calcium Lactate, $C_6H_{10}CaO_6, 5H_2O$.

NOTE—An equivalent amount of Calcium Lactate with less water of hydration may be used in place of $C_6H_{10}CaO_6, 5H_2O$ *in preparing Calcium Lactate Tablets.*

Identification : (A) Extract a quantity of the powdered tablets with *water*, filter and acidify the aqueous extract with *sulphuric acid*, add *potassium permanganate* and warm; odour of acetaldehyde is produced.

(B) The powdered tablets, when moistened with *hydrochloric acid* and introduced on a platinum wire into the flame of a Bunsen burner, gives a brick-red colour to the flame.

Disintegration : Maximum time, thirty minutes, Appendix 5.6.1.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 0.3 g of Calcium Lactate, dissolve as completely as possible in 50 ml of *water* and complete the **Assay** described under Calcium Gluconate, beginning at the words "add 5.0 ml of *0.05M magnesium sulphate*.....". Each ml of the remainder is equivalent to 0.01542 g of $C_6H_{10}CaO_6, 5H_2O$.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Storage : Store in tightly-closed containers.

Labelling : The label on the container states the quantity of calcium lactate in terms of calcium lactate pentahydrate.

Calcium Levulinate

$(CH_3COCH_2CH_2COO^-)_2Ca^{2+}, 2H_2O$

$C_{10}H_{14}CaO_6, 2H_2O$ Mol. Wt. 306.33

Category : Calcium replenisher.

Dose : 1 g daily.

Description : White, crystalline or amorphous powder; odour, faint and suggestive of burnt sugar; taste, bitter and salty.

Solubility : Freely soluble in *water*; slightly soluble in *alcohol*; insoluble in *solvent ether* and in *chloroform.*

Standards : Calcium Levulinate is the dihydrate of calcium 4-oxopentanoate. It contains not less than 97.5 per cent and not more than the equivalent of 100.5 per cent of $C_{10}H_{14}CaO_6$, calculated with reference to the dried substance.

Identification : (A) Dissolve 0.5 g in 5 ml of *water*, add 5 ml of *sodium hydroxide solution* and filter. To the filtrate add 5 ml of *iodine solution*; a precipitate of iodoform is produced.

(B) Dissolve 0.1 g in 2 ml of *water*, add 5 ml of *dinitrophenylhydrazine solution* and allow the mixture to stand in an ice-bath for one hour. Collect the precipitate on a filter, wash well with cold *water* and dry at 105° for one hour; the residue so obtained melts between 198° and 206°, Appendix 5.11.

(C) A solution (1 in 10) gives the reactions of *calcium*, Appendix 3.1.

Melting range : Between 119° and 125°, Appendix 5.11.

pH : Between 7.0 and 8.5, determined in a 10.0 per cent w/v solution, Appendix 5.10.

Arsenic : Not more than 3 parts per million, Appendix 3.2.1.

Heavy metals : Not more than 20 parts per million, determined on 1.0 g by Method A, Appendix 3.2.4.

Reducing sugars : Dissolve 0.5 g in 10 ml of *water*, add 2 ml of *dilute hydrochloric acid*, boil for about ten minutes, and cool. Add 5 ml of *sodium carbonate solution*, allow to stand for five minutes, dilute with *water* to 20 ml, and filter. Add 5 ml of the clear filtrate to about 2 ml of *potassium cupri-tartrate solution*, and boil for one minute; no red precipitate is formed immediately.

Loss on drying : Between 10.5 per cent and 12.0 per cent, determined on 0.5 g by drying "in vacuo at 60°" for five hours, Appendix 5.8.

Assay : Weigh accurately about 0.6 g, dissolve in 50 ml of *water* and complete the **Assay** described under Calcium Gluconate, beginning at the words "add 5 ml of *0.05M magnesium sulphate*.....". Each ml of the remainder is equivalent to 0.01351 g of $C_{10}H_{14}CaO_6$.

Storage : Store in well-closed containers.

Calcium Levulinate Injection

Category : Calcium replenisher.

Dose : Calcium Levulinate, by intramuscular or intravenous injection, 1 g once a day.

Usual strength : 100 mg per ml.

Standards : Calcium Levulinate Injection is a sterile solution of Calcium Levulinate in Water for Injection. It contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Calcium Levulinate, $C_{10}H_{14}CaO_6, 2H_2O$.

Identification : (A) It gives the reactions of *calcium*, Appendix 3.1.

(B) To a volume equivalent to 500 mg of Calcium Levulinate, add 5 ml of *sodium hydroxide solution* and filter. To the filtrate add 5 ml of *iodine solution*; a precipitate of iodoform is produced.

(C) To a volume equivalent to 100 mg of Calcium Levulinate add 5 ml of *dinitrophenylhydrazine solution*, and allow the mixture to stand in an ice-bath for one hour; collect the precipitate on a filter, wash well with cold *water*, and dry at 105°, for one hour; the hydrazone so obtained melts between 198° and 206°, Appendix 5.11.

pH : Between 7.0 and 8.5, Appendix 5.10.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using a volume equivalent to 200 mg of Calcium Levulinate per kg of the rabbit's weight.

Other requirements : Complies with the requirements stated under Injections.

Assay : To a volume equivalent to 0.6 g of Calcium Levulinate, add 50 ml of *water* and complete the **Assay** described under Calcium Gluconate. Each ml of the remainder is equivalent to 0.01532 g of $C_{10}H_{14}CaO_6$, $2H_2O$.

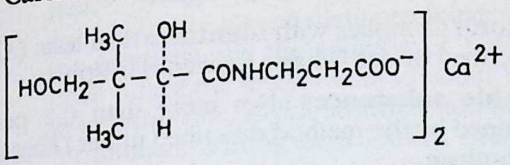
Storage : Store in single-dose containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Calcium Pantothenate

Calcium D Pantothenate



$C_{18}H_{32}CaN_2O_{10}$ Mol. Wt. 476.54

Category : Vitamin B (enzyme co-factor).

Dose : 10 to 100 mg, daily.

Description : White powder; odourless; taste, bitter. Slightly hygroscopic.

Solubility : Freely soluble in *water*; soluble in *glycerin*; practically insoluble in *alcohol*, in *chloroform* and in *solvent ether.*

Standards : Calcium Pantothenate is the calcium salt of the dextrorotatory isomer of (*R*)-3-(2,4-dihydroxy-3,3-dimethylbutyramido) propionic acid (pantothenic acid). It contains not less than 90.0 per cent and not more than the equivalent of 110.0 per cent of dextrorotatory calcium pantothenate, calculated with reference to the dried substance.

Identification : (A) A solution (1 in 20) gives the reactions of *calcium*, Appendix 3.1.

(B) Boil 50 mg in 5 ml of *N sodium hydroxide* for one minute, cool and add 5 ml of *N hydrochloric acid* and two drops of *ferric chloride test-solution*; a strong yellow colour is produced.

(C) To 50 mg in 2 ml of *N sodium hydroxide* add 0.1 ml of *copper sulphate solution*; a blue colour is produced.

Specific optical rotation : Between +25.0° and +27.5°, determined in a 5.0 per cent w/v solution, Appendix 5.12.

pH : Between 7.0 and 9.0, determined in a 5.0 per cent w/v solution, Appendix 5.10.

Heavy metals : Not more than 40 parts per million, determined by Method A on 0.5 g dissolved in 25 ml of *water*, Appendix 3.2.4.

Calcium : Between 8.2 per cent and 8.6 per cent, calculated with reference to the dried substance and determined by the following method: Weigh accurately about 0.8 g and dissolve in 50 ml of *water*. Complete the **Assay** described under Calcium Gluconate, beginning at the words "add 5 ml of *0.05M magnesium sulphate* ....". Each ml of the remainder is equivalent to 0.002004 g of Ca.

Nitrogen : Between 5.7 per cent and 6.0 per cent, calculated with reference to the dried substance and determined by the following method: Carry out the *determination of nitrogen*, Appendix 3.3.5, using about 0.5 g, accurately weighed. Each ml of *0.1N sulphuric acid* is equivalent to 0.001401 g of N.

Loss on drying : Not more than 5.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Carry out the *assay of calcium pantothenate*, Appendix 4.2.

Storage : Store in well-closed containers.

Dibasic Calcium Phosphate

$CaHPO_4$ Mol. Wt. 136.06

$CaHPO_4, 2H_2O$ Mol. Wt. 172.09

Category : Calcium supplement, pharmaceutical aid (excipient).

Dose : 1 to 5 g.

Description : White powder; odourless; tasteless.

Solubility : Practically insoluble in *water* and in *alcohol*; soluble in *dilute hydrochloric acid* and in *dilute nitric acid.*

Standards : Dibasic Calcium Phosphate is anhydrous or contains two molecules of water of hydration. It contains not less than 30.9 per cent and not more than 31.7 per cent of calcium, Ca, calculated with reference to the ignited substance.

Identification : (A) Warm 0.1 g with 5 ml of *dilute hydrochloric acid* and 5 ml of *water* till it dissolves; the solution gives the reactions of *calcium*, Appendix 3.1.

(B) Dissolve 0.1 g in a slight excess of warm *dilute nitric acid*; the solution gives the reactions of *phosphates*, Appendix 3.1.

Acid-insoluble substances : Not more than 0.1 per cent, determined by the following method: Heat 5 g with a mixture of 40 ml of *water* and 10 ml of *hydrochloric acid* until no more dissolves, and dilute to 100 ml with *water*. Filter, wash with hot *water* until the last washing is free from chloride, and dry the residue at 105° for one hour.

pH : Between 6.0 and 7.0, determined in a 20 per cent w/v suspension in *water*, Appendix 5.10.

Carbonate : Suspend 1 g in 5 ml of *water* and add 2 ml of *hydrochloric acid*; no effervescence is produced.

Iron : Dissolve 0.1 g in a mixture of 5 ml of *water* and 0.5 ml of *iron-free hydrochloric acid* with the addition of 1 g of *citric acid*. Dilute the solution to 40 ml with *water*; the resulting solution complies with the *limit test for iron*, Appendix 3.2.5.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Chloride : Dissolve 0.3 g in *water* by the addition of 2 ml of *nitric acid*; the solution complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphate : Dissolve 0.1 g in *water* by the addition of 1 ml of *hydrochloric acid*; the solution complies with the *limit test for sulphates*, Appendix 3.2.8.

Arsenic : Not more than 10 parts per million, Appendix 3.2.1.

Heavy metals : Not more than 30 parts per million, determined by Method A on 1.0 g warmed with 3 ml of *dilute hydrochloric acid*, cooled and diluted to 50 ml with *water*, Appendix 3.2.4.

Loss on drying : Not more than 1.0 per cent determined on 1.0 g by drying "in vacuo at 60°" for three hours, Appendix 5.8.

Loss on ignition : Between 6.6 per cent and 8.5 per cent (for anhydrous) and between 24.5 per cent and 26.5 per cent (for the dihydrate), determined on 1.0 g by igniting in a muffle furnace at 800° to 825°

Assay : Weigh accurately about 0.2 g and dissolve with the aid of gentle heat in a mixture of 5 ml of *hydrochloric acid* and 3 ml of *water*. Add 125 ml of *water* and with constant stirring, and in the order given, add the following: 0.5 ml of *triethanolamine*, 0.3 g of *hydroxynaphthol blue indicator* and from a burette about 23 ml of *0.05M disodium ethylenediaminetetraacetate*. Add *sodium hydroxide solution* until the initial red colour changes to clear blue, then continue to add dropwise until the colour changes to violet and then add an additional 0.5 ml. Continue the titration till a clear blue end-point that persists for not less than 60 seconds is obtained. Each ml of *0.05M disodium ethylenediaminetetraacetate* is equivalent to 0.002004 g of Ca.

Storage : Store in well-closed containers.

Tribasic Calcium Phosphate

Category : Pharmaceutical aid (excipient).

Description : White, amorphous powder; odourless; almost tasteless.

Solubility : Practically insoluble in *water* and in *alcohol*; soluble in *dilute nitric acid* and in *dilute hydrochloric acid*.

Standards : Tribasic Calcium Phosphate consists of a variable mixture of calcium phosphates having the approximate composition $10CaO, 3P_2O_5, H_2O$. It contains not less than 34.0 per cent and not more than 40.0 per cent of calcium, Ca, and an amount of phosphate, PO_4, equivalent to not less than 90.0 per cent of calcium phosphate, $Ca_3(PO_4)_2$, calculated with reference to the ignited substance.

Identification : Complies with **Identification** tests (A) and (B) described under Dibasic Calcium Phosphate.

Acid-insoluble substances : Not more than 0.2 per cent, determined by the method described under Dibasic Calcium Phosphate.

Water-soluble substances : Not more than 0.5 per cent, determined by the following method: Digest 2.0 g with 100 ml of *water* for thirty minutes on a water-bath, cool, add sufficient *water* to restore the original volume, stir well and filter. Evaporate 50 ml of the filtrate to dryness and dry the residue at 105° to constant weight.

Carbonate : Suspend 5 g in 50 ml of *water* and add 10 ml of *hydrochloric acid*; no effervescence is produced.

Chloride : Dissolve 0.1 g in 25 ml of *water* by the addition of 1 ml of *nitric acid*; the solution complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphate : Dissolve 0.15 g in 25 ml of *water* by the addition of 1 ml of *hydrochloric acid*; the solution complies with the *limit test for sulphates*, Appendix 3.2.8.

Arsenic : Not more than 5 parts per million, Appendix 3.2.1.

Heavy metals : Not more than 30 parts per million, determined by Method A on 25 ml of the solution prepared in the following manner. Warm 1 g with 4 ml of *dilute hydrochloric acid* until no more dissolves, add sufficient *water* to produce 50 ml and filter, Appendix 3.2.4.

Iron : Dissolve 0.1 g in a mixture of 5 ml of *water* and 0.5 ml of *iron-free hydrochloric acid* with the addition of 1 g of *citric acid*. Dilute the solution to 40 ml with *water*; the solution complies with the *limit test for iron*, Appendix 3.2.5.

Dibasic salt and calcium oxide : Weigh accurately about 2 g and dissolve by warming with 50.0 ml of *N hydrochloric acid*. Cool, and slowly titrate with *N sodium hydroxide* shaking constantly, to a pH of 4.0, determined potentiometrically. Not less than 13.0 ml and not more than 14.3 ml of *N hydrochloric acid* is consumed for each g, calculated with reference to the ignited substance.

Water : Not more than 2.5 per cent w/w, Appendix 3.3.25.

Loss on ignition : Not more than 8.0 per cent, determined on 1.0 g by igniting in a muffle furnace at 800° for thirty minutes.

Assay : (a) *For calcium* — Weigh accurately about 0.15 g and complete the **Assay** as described under Dibasic Calcium Phosphate, beginning at the words "dissolve with the gentle heat.....".

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

(b) *For phosphate, PO_4* – Weigh accurately about 0.2 g and dissolve in a mixture of 25 ml of *water* and 10 ml of *dilute nitric acid*. Filter and wash any precipitate with *water*. To the filtrate add sufficient *strong ammonia solution*, to produce a slight precipitate, and then dissolve the precipitate by the addition of 1 ml of *dilute nitric acid*. Adjust the temperature to about 50°, add 75 ml of *ammonium molybdate solution*, and heat at about 50° for 30 minutes, stirring occasionally. Wash the precipitate once or twice with 30 ml quantities of *water* by decantation. Transfer the precipitate to a filter paper, and wash with a 1 per cent w/v solution of *potassium nitrate* until the last washing is not acid to *litmus paper*. Transfer the precipitate and filter paper to the precipitation vessel with 50 ml of *water*, add 40.0 ml of *N sodium hydroxide*, agitate until the precipitate is dissolved, add *phenolphthalein solution* and titrate the excess alkali with *N sulphuric acid*. Each ml of *N sodium hydroxide* is equivalent to 0.006743 g of $Ca_3(PO_4)_2$.

Storage : Store in well-closed containers.

Capsules

Capsules are solid dosage forms in which the drug or mixture of drugs is enclosed in a hard or a soft, soluble, "shell" of gelatin or any other suitable material. They are intended for oral administration.

The consistency of capsule shells may be adjusted by the addition of substances such as Glycerin and Sorbitol or a mixture of these. Excipients such as opaque fillers, antimicrobial preservatives, sweetening agents, flavouring agents and one or more colouring agents permitted under the Drugs and Cosmetics Rules may be added. Capsules may bear surface markings.

The contents of capsules may be of solid, liquid or paste-like consistency. They consist of one or more medicaments with or without excipients such as solvents, diluents, lubricants, fillers, wetting agents and disintegrating agents. They do not contain any added colouring agent.

Hard capsules : Hard capsule shells consist of two prefabricated cylindrical sections, one end of which is rounded and sealed, and the other is open. The contents of the capsules are filled into one of the sections which is then closed by slipping the other section over it. The closure can be strengthened by suitable means.

Hard gelatin capsule sizes range from No. 5, the smallest to No. 000 which is the largest. The shells normally contain between 10 and 15 per cent of water. They should be stored in tightly-closed containers and protected from potential sources of microbial contamination.

The contents of hard capsules usually consist of the medicament or mixture of medicaments in the form of powder, beads or granules. Where two mutually incompatible drugs are present in the mixture, one of the drugs can be put in a small capsule and then enclosed with the other drug in a large capsule or alternatively the drugs can be separated by placing pellets, tablets or soft capsules of one drug into the hard capsule shell before adding the other drug. After filling the madicament the surface of the finished capsule should be cleaned and freed from the drug contained therein.

Soft capsules : Soft capsule shells are usually formed, filled with medicament and sealed in a combined operation on machines. The shells which are thicker than those of hard capsules are formed to produce capsules which are spherical, oval or cylindrical with hemispherical ends. The shells may sometimes contain a medicament. They may contain a preservative to prevent growth of fungi.

The contents of soft capsules usually consist of liquids or solids dissolved or dispersed in suitable excipients to give a paste-like consistency, but may also consist of powders or granules. As soft gelatin shells contain appreciable amounts of water, migration of capsule contents, particularly of water-soluble ingredients, may occur.

Requirements of tests : Hard and soft capsules comply with the following requirements:

(1) *Content of active ingredients in capsules*– Determine the amount of active ingredient by the method in the assay; calculate, if necessary, the amount of active ingredient in the capsules taken for the assay and divide by the number of capsules. The result lies within the range for the content of active ingredient stated in the monograph. This range is based on the requirement that 20 capsules, or such other number as may be indicated in the monograph, are used in the assay. Where 20 capsules cannot be obtained, a smaller number, which must not be less

TABLE 1

Weight of medicament in each capsule	Subtract from the lower limit for samples of			Add to the upper limit for samples of		
	15	10	5	15	10	5
0.12 g or less	0.2	0.7	1.5	0.3	0.8	1.8
More than 0.12 g and less than 0.3 g	0.2	0.5	1.2	0.3	0.6	1.5
0.3 or more	0.1	0.2	0.8	0.2	0.4	1.0

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

than 5, may be used; in such cases the limits specified in the monograph may be relaxed to the extent indicated in Table 1. The requirements of this Table apply when the stated limits are between 90 and 110 per cent. For limits less than 90 or greater than 110 per cent, proportionately larger allowance should be made.

(2) *Uniformity of weight*—Weigh 20 intact capsules individually and determine the average weight. The individual weights are between 90 per cent and 110 per cent of the average weight. If all of the capsules do not fall within these limits carry out the following test: Weigh an intact capsule. Open the capsule without losing any part of the shell, and remove the contents as completely as possible. For soft capsules, wash the shell with *solvent ether* or any other suitable solvent and allow the shell to stand at room temperature until the odour of the solvent is no longer perceptible. Weigh the shell. The weight of the contents is the difference between the weighings. Repeat the procedure with a further nineteen capsules. Determine the average weight of the contents. Not more than two of the individual weights deviate from the average by more than the percentage deviation shown in Table 2 and none deviates by more than twice that percentage.

If more than two but not more than six capsules deviate from the average between the precentage deviation shown in Table 2 and twice that percentage, determine the weight of contents of an additional 40 capsules and the average content of the 60 capsules. In not more than six of the capsules does the individual weight deviate from the average by more than the percentage deviation shown in Table 2 and none deviates by more than twice that percentage.

TABLE 2

Average weight of capsule contents	Percentage of deviation
Less than 300 mg	10
300 mg or more	7.5

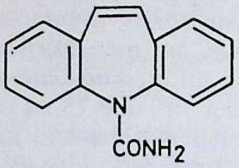
(3) *Disintegration*—Comply with the *disintegration test for capsules*, Appendix 5.6.2.

General Requirements

Storage : Capsules should be stored in tightly-closed containers at temperatures not exceeding 30°. They should also comply with such additional storage requirements as are specified in the individual monograph.

Labelling : Comply with the general requirements for Labelling and with such other requirements as are specified in the individual monograph.

Carbamazepine



$C_{15}H_{12}N_2O$ Mol. Wt. 236.27

Category : Analgesic (specific in trigeminal neuralgia).

Dose : 0.2 g daily, increasing to 1.2 g daily, in divided doses, in accordance with the needs of the patient.

Description : White or yellowish white, crystalline powder; almost odourless; taste, slightly bitter.

Solubility : Practically insoluble in *water*; soluble in *alcohol*, and in *chloroform*; almost insoluble in *solvent ether*.

Standards : Carbamazepine is 5*H*-dibenz (b,f) azepine-5-carboxamide. It contains not less than 97.0 per cent and not more than the equivalent of 103.0 per cent of $C_{15}H_{12}N_2O$, calculated with reference to the dried substance.

Identification : (A) Heat 0.1 g with 2 ml of *nitric acid* in a water-bath for three minutes; an orange-red colour is produced.

(B) The light absorption, in the range 230 to 300 nm, of a 1-cm layer of a 0.001 per cent w/v solution in *alcohol* exhibits a maximum only at 285 nm; *extinction* at 285 nm, about 0.49, Appendix 5.15 A.

(C) Exhibits an intense blue fluorescence in ultra-violet light at 366 nm.

Melting range : Between 189° and 193°, Appendix 5.11.

Acidity or Alkalinity : Stir 1.0 g with 20 ml of *water* for fifteen minutes and filter. Titrate 10 ml of the filtrate with *0.1N sodium hydroxide* using one drop of *phenolphthalein solution* as indicator; not more than 0.5 ml is required. Add three drops of a 0.05 per cent w/v solution of *methyl red* and titrate with *0.01N hydrochloric acid* until the colour changes to red; not more than 1.0 ml is required.

Chloride : 2.0 g complies with the *limit test for chlorides*, Appendix 3.2.2.

Heavy metals : Not more than 10 parts per million, determined on 2.0 g by Method B, Appendix 3.2.4.

Foreign substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using a suitable silica gel as the coating substance and a mixture of 95 volumes of *toluene* and 5 volumes of *methyl alcohol* as

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

the mobile phase. Apply separately to the plate 10 µl of (1) a 2.5 per cent w/v solution in *chloroform* of the substance being examined; (2) a 0.005 per cent w/v solution of *iminodibenzyl R.S.* in *methyl alcohol*. After removal of the plate allow it to dry in air for fifteen minutes and spray with a 0.5 per cent w/v solution of *potassium dichromate* in a mixture of 1 volume of *sulphuric acid* and 4 volumes of *water*. Any spot in the chromatogram obtained with solution (1), other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (2).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105° for two hours, Appendix 5.8.

Assay : Weigh accurately about 0.1 g and dissolve in sufficient *alcohol* to produce 100.0 ml. Dilute 10.0 ml to 100.0 ml with *alcohol* and dilute 10.0 ml of the dilution to 100.0 ml with *alcohol*. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 285 nm, Appendix 5.15 A. Calculate the content of $C_{15}H_{12}N_2O$, taking 490 as the value of E(1 per cent, 1-cm) at the maximum at about 285 nm.

Storage : Store in well-closed containers.

Carbamazepine Tablets

Category : Analgesic (specific in trigeminal neuralgia).

Dose : Carbamazepine, 0.2 g daily, increasing to 1.2 g daily, in divided doses, in accordance with the needs of the patient.

Usual strength : 0.2 g.

Standards : Carbamazepine Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Carbamazepine, $C_{15}H_{12}N_2O$.

Identification : (A) Boil a quantity of the powdered tablets equivalent to 0.2 g of Carbamazepine with 15 ml of *acetone*, filter the hot solution, wash the filter with the two quantities, each of 5 ml, of hot *acetone*, evaporate the combined filtrates to 5 ml, and cool to 0°. The crystals, after washing with *acetone* and drying "in vacuo at 70°" for thirty minutes, melt at about 191°, Appendix 5.11, and comply with **Identification** test (A) described under Carbamazepine.

(B) The powdered tablets exhibit an intense blue fluorescence in ultra-violet light at 366 nm.

Foreign substances : Comply with the test described under Carbamazepine, using instead of solution (1) a solution prepared in the following manner: Shake a quantity of the powdered tablets equivalent to 0.2 g of Carbamazepine with three quantities, each of 10 ml, of *chloroform* and filter; evaporate the combined filtrates to dryness and dissolve the residue in 10 ml of *chloroform*. Use for solution (2) a 0.006 per cent w/v solution of *iminodibenzyl R.S.* in *methyl alcohol*.

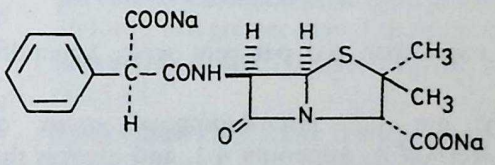
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 60 mg of Carbamazepine and boil in a flask with 25 ml of *alcohol* for a few minutes, stir the hot mixture in the closed flask for ten minutes and filter through a sintered glass funnel, washing the flask and funnel with *alcohol* and adding sufficient *alcohol* to the cooled filtrate to produce 100.0 ml. Dilute 5.0 ml to 250.0 ml with *alcohol* and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 285 nm, Appendix 5.15 A. Calculate the content of the $C_{15}H_{12}N_2O$, taking 490 as the value of E(1 per cent, 1-cm) at the maximum at about 285 nm.

Storage : Store in well-closed containers.

Carbenicillin Disodium

Carbenicillin Sodium



$C_{17}H_{16}N_2Na_2O_6S$ Mol. Wt. 422.36

Category : Antibacterial.

Dose : By intravenous injection, the equivalent of 12 to 30 g of carbenicillin daily, in divided doses.

By intramuscular injection, the equivalent of 4 to 8 g of carbenicillin daily in divided doses.

Description : White or almost white powder; odourless; taste, bitter; hygroscopic.

Solubility : Freely soluble in *water*; soluble in *alcohol*; practically insoluble in *chloroform* and in *solvent ether*.

Standards : Carbenicillin Disodium is the disodium salt of (6*R*)-6-[(*F*)-2-carboxy-2-phenylacetamido]-penicillanic acid. It contains the equivalent of not less than 770 µg of carbenicillin per mg, calculated with reference to the anhydrous substance.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *carbenicillin disodium R.S.*, Appendix 5.15 B.

(B) Heat 0.5 g in a small sealed container on a water-bath for three minutes, remove the seal, and immediately replace by a cork fitted with a platinum loop carrying a drop of a solution freshly prepared by mixing 1 ml of a 0.5 per cent w/v solution of *sodium carbonate*, 1 ml of *phenolphthalein solution* and 10 ml of *water*; the reagent is decolorised within two minutes.

(C) A solution (1 in 20) gives the reactions of *sodium*, Appendix 3.1.

Specific optical rotation : Between +182° and +196°, determined at 20° in a 1.0 per cent w/v solution, Appendix 5.12.

pH : Between 6.0 and 8.0, determined in a 10 per cent w/v solution, Appendix 5.10.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using not less than 6 mg per kg of the rabbit's weight, dissolved in not more than 5 ml of *water for injection*.

Sterility : Complies with the *tests for sterility*, Appendix 4.6.

Undue toxicity : Complies with the test described under Bacitracin, using 20 mg dissolved in 0.5 ml of *water for injection*, the injection occupying not more than sixty seconds.

Water : Not more than 6.0 per cent w/w, Appendix 3.3.25.

Assay : Carry out the *microbiological assay of antibiotics, Method A*, Appendix 4.1, and express the result in µg of carbenicillin per mg.

Storage : Store in sterile containers, sealed so as to exclude micro-organisms and at a temperature not exceeding 5°.

Labelling : The label on the container states (1) the date after which the contents are not intended to be used; (2) the storage conditions.

Carbenicillin Injection

Category : Antibacterial.

Dose : By intravenous injection, the equivalent of 12 to 30 g of carbenicillin daily, in divided doses.

By intramuscular injection, the equivalent of 4 to 8 g of carbenicillin daily in divided doses.

Usual strengths : The equivalent of 1 g and 5 g of carbenicillin.

Standards : Carbenicillin Injection is a sterile solution of Carbenicillin Disodium in Water for Injection. It is prepared by dissolving the contents of a sealed container in the requisite amount of Water for Injection, immediately before use.

Content of Carbenicillin Disodium, $C_{17}H_{16}N_2Na_2O_6S$: Determine the weight of the contents of each of ten containers as described in the test for **Uniformity of weight** under Injections. From the result of the Assay calculate the proportionate amount of carbenicillin, $C_{17}H_{18}N_2O_6S$, in each container; each mg of carbenicillin disodium, $C_{17}H_{16}N_2Na_2O_6S$ is equivalent to 0.896 mg of carbenicillin, $C_{17}H_{18}N_2O_6S$. This amount does not deviate from the amount stated on the label by a greater percentage than that shown in column A of the Table of Deviations, except that in one container the amount may deviate by not more than twice the percentage shown.

Other requirements : Complies with the requirements stated under Injections.

The contents of the sealed container comply with the following requirements:

Description : White or almost white powder; odourless.

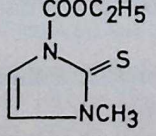
Identification; Specific optical rotation; pH; Pyrogens; Sterility; Undue toxicity and Water : Comply with the requirements stated under Carbenicillin Disodium.

Assay : Carry out the **Assay** described under Carbenicillin Disodium, using the mixed contents of ten containers.

Storage : Store at a temperature not exceeding 5° The constituted solution should be used immediately after preparation.

Labelling : The label on the container states (1) the quantity of Carbenicillin Disodium contained in it in terms of the equivalent amount of carbenicillin; (2) the date after which the contents are not intended to be used; (3) the storage conditions.

Carbimazole



$C_7H_{10}N_2O_2S$ Mol. Wt. 186.23

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Category : Antithyroid substance.

Dose : Controlling dose, 30 to 60 mg daily, in divided doses; maintenance dose, 5 to 20 mg daily.

Description : White or creamy-white, crystalline powder; odour, characteristic; tasteless at first, followed by a bitter taste.

Solubility : Freely soluble in *chloroform*; soluble in *acetone*; sparingly soluble in *alcohol*; slightly soluble in *water* and in *solvent ether*.

Standards : Carbimazole is ethyl 3-methyl-2-thioxo-4-imidazoline-1-carboxylate. It contains not less than 98.5 per cent of $C_7H_{10}N_2O_2S$, calculated with reference to the dried substance.

Identification : (A) Heat 0.2 g with 5 ml of *dilute hydrochloric acid* on a water-bath for one hour. Cool, extract with three quantities, each of 5 ml, of *chloroform*, wash the combined chloroform extracts with 0.5 ml of *water*, filter through a dry filter paper and remove the chloroform. The residue, after crystallisation from *alcohol* melts at about 140°, Appendix 5.11.

(B) To a small quantity add one drop of *dilute potassium iodobismuthate solution*; a scarlet colour is produced.

Melting range : Between 122° and 125°, Appendix 5.11.

Methimazole : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 4 volumes of *chloroform* and 1 volume of *acetone* as the mobile phase. Apply separately to the plate 10 µl of each of the two solutions in *chloroform* containing (1) 1.0 per cent w/v of the substance being examined and (2) 0.005 per cent w/v of *methimazole R.S.* and develop immediately. After removal of the plate, allow it to dry in air and spray with *dilute potassium iodobismuthate solution*. The spot in the chromatogram obtained with solution (2) is more intense than any corresponding spot in the chromatogram obtained with solution (1).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent determined on 1.0 g by drying "in vacuo" for twenty-four hours, Appendix 5.8.

Assay : Weigh accurately about 50 mg and dissolve in sufficient *water* to produce 500.0 ml. To 10.0 ml of the solution, add 10 ml of *N hydrochloric acid* and sufficient *water* to produce 100.0 ml and measure the *extinction* of a 1-cm layer of the resulting solution at 291 nm, Appendix 5.15 A. Calculate the content of $C_7H_{10}N_2O_2S$, taking 557 as the value of E(1 per cent, 1-cm) at 291 nm.

Storage : Store in well-closed containers.

Castor Oil

Category : Cathartic; Pharmaceutical aid (plasticizer).

Dose : 1 to 15 ml.

Description : Pale yellowish or almost colourless, transparent, viscid liquid; odour, slight and characteristic; taste, at first bland, but afterwards slightly acrid.

Solubility : Soluble in *alcohol*; miscible with *ethyl alcohol*, with *chloroform*, with *solvent ether*, and with *glacial acetic acid*.

Standards : Castor Oil is the fixed oil obtained by cold expression from the seeds of *Ricinus communis* Linn. (Fam. Euphorbiaceae).

Identification : (A) Mixes completely with half its volume of *light petroleum (boiling range 40 ° to 60 °)* and is only partially soluble in two volumes.

(B) Add to an equal volume of *alcohol*; a clear liquid is obtained; cool to 0° for three hours; the liquid remains clear (distinction from other fixed oils).

Wt. per ml : Between 0.945 and 0.965 g, Appendix 5.19.

Optical rotation : Between +3.5° and +6.0°, Appendix 5.12.

Light absorption : *Extinction* of a 1-cm layer of a 1.0 per cent w/v solution in *alcohol* at the maximum at about 269 nm, not greater than 1.0, Appendix 5.15 A.

Refractive index : Between 1.4758 and 1.4798, Appendix 5.14.

Acid value : Not more than 2.0, Appendix 3.3.15.

Iodine value : Between 82 and 90, Appendix 3.3.18.

Saponification value : Between 176 and 187, Appendix 3.3.20.

Acetyl value : Not less than 143, Appendix 3.3.14.

Peroxide value : Not more than 5.0, Appendix 3.3.19.

Water : Not more than 0.3 per cent w/w, Appendix 3.3.25.

Storage : Store in well-closed and well-filled, light-resistant containers, in a cool place.

Microcrystalline Cellulose

Category : Pharmaceutical aid (suspending agent; tablet and capsule diluent).

Description : Coarse to fine, white or off-white, crystalline powder; odourless; tasteless.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Microscopical – Mounted in *lactophenol* the non-dispersible type exhibits particles of various sizes an irregular shapes, many pieces about 100 to 150 µm long and 20 to 30 µm wide, showing numerous cracks and a rather irregular outline and also many minute particles about 10 to 15 µm in width or length and marked with short irregular lines.

The particles of the colloidal type are similar in appearance but smaller, most being about 12 to 15 µm or occasionally upto 18 µm, and some rather square, about 40µm, somewhat elongated, about 50µm by 10 µm, to 20µm.

Between crossed polars on a dark field the material shines brightly.

Crystalline structures are absent.

Solubility : Insoluble in dilute acids and in most organic solvents. Swells in *water*, producing, when dispersed, a white, opaque dispersion or gel. Slightly soluble in *dilute sodium hydroxide solution.*

Standards : Microcrystalline Cellulose is purified, partially depolymerised cellulose prepared by treating alpha cellulose, obtained as a pulp from fibrous plant material, with mineral acids. It contains not less than 97.0 per cent and not more than the equivalent of 102.0 per cent of cellulose, calculated, with reference to the dried substance.

Identification : (A) To about 1 mg add about 1 ml of *phosphoric acid*, heat on a water-bath for 30 minutes, add 4 ml of a 0.2% w/v solution of *catechol* in *phosphoric acid*, and heat for further 30 minutes; a red colour is produced.

(B) To 50 mg add 2 ml of *iodine solution*, allow to stand for five minutes and remove the excess reagent with the aid of a filter paper and add one or two drops of *dilute sulphuric acid*; a blue-purple colour is produced.

pH : Between 5.0 and 7.0, determined on the supernatant liquid obtained by shaking 5 g with 40 ml of *water* for twenty minutes and centrifuging, Appendix 5.10.

Starch : Mix 30 g with 270 ml of *water* in a high-speed (10,000 r.p.m. or more) power blender for five minutes. To 20 ml of the dispersion add two to three drops of *iodine solution*, and mix; no purplish blue or blue colour is produced.

Organic impurities : Place 10 mg on a watch-glass and add 0.05 ml of a freshly-prepared solution of 0.1 g of *phloroglucinol* in 5 ml of *hydrochloric acid*; no red colour is produced.

Water-soluble substances : Not more than 0.16 per cent, determined by the following method: Shake 5.0 g with about 80 ml of *water* for ten minutes and filter through filter paper (Whatman No. 42 or equivalent) into a tared beaker, evaporate on a water-bath to dryness and dry at 105° for one hour.

Arsenic : Not more than 2 parts per million, Appendix 3.2.1.

Heavy metals : Not more than 10 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

Sulphated ash : Not more than 0.2 per cent, Appendix 3.2.7.

Loss on drying : Not more than 5.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.125 g and transfer to a 300 ml conical flask with the aid of about 25 ml of *water*. Add 50.0 ml of *0.5N potassium dichromate*, mix, carefully, add 100 ml of *sulphuric acid* and heat to boiling. Remove from heat, allow to stand at room temperature for fifteen minutes, cool and transfer to a 250-ml volumetric flask. Dilute with *water* almost to volume, cool to 25°, dilute with *water* to volume and mix. Titrate a 50 ml aliquot with *0.1N ferrous ammonium sulphate*, using 2 to 3 drops of *orthophenanthroline solution* as indicator. Perform a blank determination using 50.0 ml of the same *0.5N potassium dichromate*, and note the difference in volumes required. Each ml of the difference in volumes of *0.1N ferrous ammonium sulphate* consumed is equivalent to 0.00338 g of cellulose.

Storage : Store in well-closed containers.

Cellulose Acetate Phthalate

Cellacephate

Category : Pharmaceutical aid (enteric coating of tablets)

Description : White, free-flowing powder or colourless flakes; odourless or with a faint odour of acetic acid; tasteless; hygroscopic.

Solubility : Freely soluble in *acetone*; soluble in *diethylene glycol* and in *dioxan*; insoluble in *water* and in *alcohol.*

Standards : Cellulose Acetate Phthalate is a cellulose, some of the hydroxyl groups of which are esterified by acetyl groups and other hydroxyl groups of which are esterified by hydrogen phthalate groups. It contains not less than 17.0 per cent and not more than 23.0 per cent of acetyl (C_2H_3O) groups, and not less than 30.0 per cent and not more than 40.0 per cent of phthalyl ($C_8H_5O_3$) groups both calculated with reference to the anhydrous, acid-free substances.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Identification : (A) To about 10 mg add 1 ml of *alcohol* and 1 ml of *sulphuric acid*, and warm; ethyl acetate, recognizable by its characteristic odour, is evolved.

(B) To about 10 mg, contained in a small test-tube add 10 mg of *resorcinol*, mix, add 0.5 ml of *sulphuric acid* and heat in a liquid paraffin bath at 160° for 3 minutes. Cool and pour the solution into a mixture of 25 ml of *sodium hydroxide solution* and 200 ml of *water*. The solution shows a vivid green fluorescence.

(C) Dissolve about 100 mg in 1 ml of *acetone* and pour into a glass plate; a glossy, clear film is deposited as acetone evaporates.

Viscosity : Between 50 cP and 90 cP, determined in the following manner: Weigh accurately about 15 g, previously dried at 105° for two hours, and dissolve in 85 g, of a mixture of 249 parts of *dry acetone* and 1 part of *water*. Determine at 25° the viscosity of the resulting solution in a U-tube viscometer, size C, Appendix 5.18.

Free acid : Not more than 6.0 per cent, calculated as phthalic acid with reference to the anhydrous substance and determined in the following manner: Weigh accurately 1.0 g, in fine powder and shake for five minutes with 100 ml of boiled *water*, and filter. Wash the flask and the filter, with two quantities, each of 10 ml, of *water*. Combine the filtrate and washings, add five drops of *phenolphthalein solution* and titrate with *0.1N sodium hydroxide*, until a faint pink colour is obtained. Each ml of *0.1N sodium hydroxide* is equivalent to 0.0083 g of phthalic acid.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 5.0 per cent determined on 0.5 g by drying in an oven at 105° for two hours, Appendix 5.8.

Assay : (a) *Acetyl groups*—Weigh accurately about 0.1 g and heat on a water-bath for thirty minutes with 25.0 ml of *0.1N sodium hydroxide* under reflux. Cool, add five drops of *phenolphthalein solution* and titrate with *0.1N hydrochloric acid* until the colour is discharged. Carry out a blank determination. Calculate the acetyl groups from the formula:

$$\frac{0.43\ (c-d)}{w} - (0.578\ P + 0.518\ S) \text{ per cent}$$

where

c = ml of *0.1N hydrochloric acid* used in the blank.

d = ml of *0.1N hydrochloric acid* used in the test.

w = weight in g of the sample, calculated with reference to the anhydrous substance.

P = percentage of *phthalyl groups* as determined in Assay (b).

S = percentage of free acid.

(b) *Phthalyl groups*—Weigh accurately about 0.4 g and dissolve, without heating, in 20 ml of *ethyleneglycol monomethyl ether*, previously neutralised in the presence of five drops of *phenolphthalein solution*. Titrate with *0.1N sodium hydroxide* until a faint pink colour is produced. Calculate the phthalyl groups from the formula:

$$\frac{1.49\,b}{w} - 1.795\ S \text{ per cent},$$

where

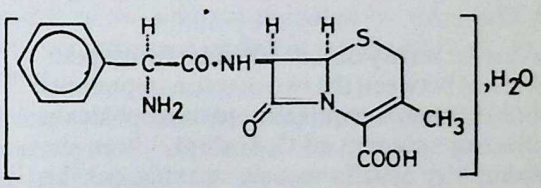
b = ml of *0.1N sodium hydroxide* used.

w = weight in g of the sample, calculated with reference to the anhydrous substance.

S = percentage of free acid.

Storage : Store in well-closed containers, in a cool place.

Cephalexin



$C_{16}H_{17}N_3O_4S, H_2O$ Mol. Wt. 365.40

Category : Antibacterial.

Dose : 1 to 4 g daily, in divided doses.

Description : White to cream-coloured, crystalline powder; odour, characteristic.

Solubility : Slightly solubie in *water*; practically insoluble in *alcohol*, in *chloroform* and in *solvent ether*.

Standards : Cephalexin is the monohydrate of 7-(D-α-aminophenyl-acetamido)-3-methyl-3-cepham-4-carboxylic acid. It contains not less than 95.0 per cent and not more than the equivalent of 103.0 per cent of $C_{16}H_{17}N_3O_4S$, calculated with reference to the anhydrous substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *cephalexin R.S.*, Appendix 5.15 B.

(B) Mix 20 mg with five drops of a 1 per cent w/v solution of *glacial acetic acid*, two drops of a 1 per cent w/v solution of *copper sulphate* ; and a few drops of *2N sodium hydroxide*; an olive-green colour is produced.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

(c) Mix 20 mg with a few drops of *sulphuric acid (80 per cent v/v)* containing 1 per cent v/v of *nitric acid*; a yellow colour is produced.

Specific optical rotation : Between +145° and +158° determined in a 1.0 per cent w/v solution in *buffer solution, pH 4.4,* and in a 2-dm tube, Appendix 5.12.

Light absorption : *Extinction* of a 1-cm layer of a 0.002 per cent w/v solution at the maximum at about 260 nm, 0.44 to 0.49, Appendix 5.15 A.

pH : Between 3.0 and 5.5, determined in a 5.0 per cent w/v solution, Appendix 5.10.

Undue toxicity : Administer orally by means of a canula or other suitable device 0.5 ml of a suspension of 5 mg in a 0.5 per cent w/v solution of *methylcellulose (4000 cps)* to each of five healthy mice, weighing between 17 to 22 g each; none of the mice dies within forty-eight hours. If one of the mice dies within forty-eight hours, repeat the test on five previously unused mice; none of the second group of mice dies within forty-eight hours.

Sulphated ash : Not more than 0.2 per cent, Appendix 3.2.7.

Water : Between 4.0 per cent and 8.0 per cent w/w, Appendix 3.3.25.

Assay : Carry out the **Assay** described under Benzylpenicillin. The difference between the two titrations represents the volume of *0.02 N iodine* equivalent to the cephalexin present. Calculate the content of $C_{16}H_{17}N_3O_4S$ from the difference obtained by simultaneously carrying out the assay using *cephalexin R.S.* instead of the substance being examined and the declared content of $C_{16}H_{17}N_3O_7S$ in *cephalexin R.S.*

Storage : Store in well-closed, light-resistant containers, in a cool place.

Labelling : The label on the container states the date after which the contents are not intended to be used; (2) the storage conditions.

Cephalexin Capsules

Category : Antibacterial.

Dose : Cephalexin, 1 to 4 g daily, in divided doses.

Usual strengths : 250 mg; 500 mg.

Standards : Cephalexin Capsules contain the equivalent of not less than 90.0 per cent and not more than 120.0 per cent of the stated amount of cephalexin, $C_{16}H_{17}N_3O_4S$.

Identification : Shake a quantity of the contents of the capsules equivalent to 0.5 g of cephalexin with 1 ml of *water* and 1.4 ml of *N hydrochloric acid*, filter, and wash the filter with 1 ml of *water*. Add slowly, to the filtrate a saturated solution of *sodium acetate* until precipitation occurs. Add 5 ml of *methyl alcohol*, filter and wash the precipitate with two quantities, each of 1 ml, of *methyl alcohol*. The residue, after drying "in vacuo", complies with the **Identification** tests described under Cephalexin.

Disintegration : Maximum time, 15 minutes, using 0.6 per cent v/v solution of *hydrochloric acid* in place of *water*, Appendix 5.6.2.

Other requirements : Comply with the requirements stated under Capsules.

Water : Not more than 10.0 per cent w/w, Appendix 3.3.25, determined on the contents of the capsules.

Assay : Mix the contents of 20 capsules and weigh. Weigh accurately a quantity of the mixed contents equivalent to about 0.25 g of Cephalexin and carry out the *microbiological assay of antibiotics. Method A*, Appendix 4.1.

Storage : Store in tightly-closed containers in a cool place.

Labelling : The label on the container states (1) the strength in terms of the equivalent amount of cephalexin; (2) the date after which the capsules are not intended to be used; (3) the storage conditions.

Cephalexin Tablets

Category : Antibacterial.

Dose : Cephalexin, 1 to 4 g daily in divided doses.

Usual strength : 250 mg.

Standards : Cephalexin Tablets contain the equivalent of not less than 90.0 per cent and not more than 120.0 per cent of the stated amount of cephalexin, $C_{16}H_{17}N_3O_4S$. The tablets may be coated.

Identification : Remove any coating. Shake a quantity of the powdered tablet cores equivalent to 0.5 g of Cephalexin with 1 ml of *water* and 1.4 ml of *N hydrochloric acid*, add 0.1 g of *decolourising charcoal*, shake, filter, and wash the filter with 1 ml of *water*. Add, slowly, to the filtrate a saturated solution of *sodium acetate* until precipitation occurs. Add 5 ml of *methyl alcohol*, filter and wash the precipitate with two quantities, each of 1 ml of *methyl alcohol*. The residue, after drying "in vacuo" complies with the **Identification** tests described under Cephalexin.

Disintegration : Maximum time 30 minutes, using 0.6 per cent v/v solution of *hydrochloric acid* in *water*, Appendix 5.6.1.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

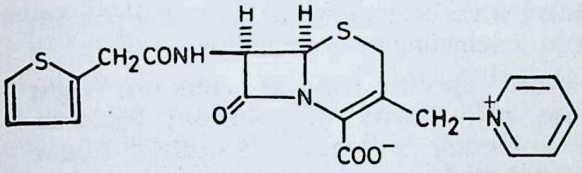
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.25 g of Cephalexin and carry out the *microbiological assay of antibiotics, Method A*, Appendix 4.1.

Storage : Store in tightly-closed containers in a cool place.

Labelling : The label on the container states (1) the strength in terms of the equivalent amount of Cephalexin; (2) the date after which the tablets are not intended to be used; (3) the storage conditions.

Cephaloridine



$C_{19}H_{17}N_3O_4S_2$ Mol. Wt. 415.48

Category : Antibacterial.

Dose : By intramuscular injection, 1 to 4 g daily, in divided doses.

Description : White or almost white crystalline powder; odour, slight, resembling that of pyridine; taste, bitter.

Solubility : Soluble in *water*; slightly soluble in *alcohol*; practically insoluble in *solvent ether* and in *chloroform*.

Standards : Cephaloridine is *N*-[7-{(2-thienyl) acetamido} ceph-3-em-3-ylmethyl]-pyridinium-4-carboxylate (α-form or δ-form). It contains not less than 95.0 per cent of $C_{19}H_{17}N_3O_4S_2$, calculated with reference to the anhydrous substance.

Identification : (A) Mix 20 mg with a few drops of a 80 per cent v/v solution of *sulphuric acid* containing 1 per cent v/v of *nitric acid*; a bluish-green colour is produced.

(B) To a 0.5 per cent solution, add 1 ml of *chloramine solution* and 2 ml of *0.1N sodium hydroxide*; a dull red colour is produced which persists for one minute.

Specific optical rotation : Between +46° and +50°, determined at 20° in a 1 per cent w/v solution, Appendix 5.12.

Light absorption : The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.002 per cent w/v solution exhibits a maximum at about 240 nm; *extinction* at the maximum at about 240 nm, 0.72 to 0.79, Appendix 5.15 A. The ratio of the *extinction* at the maximum at about 240 nm to that at about 255 nm, is not greater than 1.10.

pH : Between 4.0 and 6.0, determined on 10 per cent w/v solution prepared by dissolving in *water*, warming to 30° and then cooling to 20°, Appendix 5.10.

Clarity of solution : A solution of 0.5 g in 5 ml of *water* at 30° shows no opalescence or turbidity.

Pyridine : Dissolve 20 mg in 8 ml of *water* and 2 ml of a buffer solution prepared by adjusting a 2 per cent w/v solution of *anhydrous sodium phosphate* to pH 6.0 with *phosphoric acid* and adding a 1 per cent v/v solution of *aniline*. Add 1 ml of a solution prepared by decolourising a 0.5 per cent v/v solution of *bromine* with *potassium cyanide solution*, shaking and allowing to stand for two minutes; add sufficient *water* to produce 20 ml and allow to stand for twenty-five minutes. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 462 nm, using as the blank a solution prepared in the similar manner omitting the substance being examined, Appendix 5.15 A. The *extinction* is not more than that of the solution prepared by treating 2 ml of a 0.005 per cent w/v solution of *pyridine* in a similar manner.

Residual solvents : Carry out the method for *gas-liquid chromatography*, Appendix 5.4.1, using the following solutions in *water* containing (1) 0.25 per cent w/v of *ethyl methyl ketone* (internal standard) and 0.375 per cent w/v of *dimethylformamide* (internal standard), (2) 25 per cent w/v of the substance being examined, (3) 25 per cent w/v of the substance being examined, 0.25 per cent w/v of *ethyl methyl ketone* and 0.375 per cent w/v of *dimethylformamide*. Carry out the chromatographic procedure using (a) a glass column 1.5 m long and 0.5 cm in internal diameter packed with 10 per cent w/w of *polyethylene glycol 1000* supported on diatomaceous earth maintained at 120°, (b) nitrogen as the carrier gas, and (c) a flame ionisation detector.

Maintain the temperature of column at the point of injection at about 230° so that any pyridine produced by the degradation of cephaloridine is detected as a sharp peak. Continue the chromatographic procedure for five times the retention time of dimethylformamide. Measure the heights of the peaks or, where appropriate, their area.

In the chromatogram obtained with solution (3), the height or area of the ethyl methyl ketone peak is greater than that of the sum of the heights or areas of any other peaks with retention time less than that of pyridine; the height or area of the dimethylformamide peak is greater than the sum of the heights or areas of any other peaks with a retention time greater than that of pyridine.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using not less than 50 mg per kg of the rabbit's weight, dissolved in 1 ml of *water for injection*.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Sterility : Complies with the *test for sterility*, Appendix 4.6.

Undue toxicity : Complies with the test described under Bacitracin, using 35 mg dissolved in 0.5 ml of *water for injection* per mouse.

Sulphated ash : Not more than 0.2 per cent, Appendix 3.2.7.

Water : Not more than 0.5 per cent w/w (α-form) or not more than 3.0 per cent w/w (δ-form), Appendix 3.3.25. Use as the solvent a mixture of equal volumes of *dehydrated methyl alcohol* and *dehydrated pyridine.*

Assay : Weigh accurately about 60 mg and dissolve in sufficient *water* to produce 50.0 ml. Transfer 10.0 ml to a stoppered flask, add 5 ml of *N sodium hydroxide*, and allow to stand for twenty minutes. Add 20 ml of buffer solution containing 35.0 per cent w/v of *sodium acetate* and 42.4 per cent v/v of *glacial acetic acid*, 5 ml of *N hydrochloric acid* and 25.0 ml of *0.02 N iodine*, close the flask with a wet stopper and allow to stand for three hours in a water-bath at 30°, protected from light. Titrate the excess of iodine with *0.02 N sodium thiosulphate*, using *starch solution* towards the end of the titration, as indicator. To a further 10.0 ml of the solution add 20 ml of the buffer solution and 25.0 ml of *0.02 N iodine*, allow to stand for three hours in a water-bath at 30°, protected from light. Titrate the excess of iodine with *0.02 N sodium thiosulphate*, using *starch solution* towards the end of the titration, as indicator. The difference between the titrations represents the volume of *0.02 N iodine* equivalent to the Cephaloridine present.

Calculate the content of $C_{19}H_{17}N_3O_4S_2$ from the difference obtained by simultaneously carrying out the assay using *cephaloridine (δ-form) R.S.* instead of the substance being examined and from the declared content of $C_{19}H_{17}N_3O_4S_2$ in *cephaloridine (δ-form) R.S.*

Storage : Store in light-resistant, sterile containers, sealed so as to exclude micro-organisms and in a cool and dry place

Labelling : The label on the container states (1) whether the contents are Cephaloridine (α-form) or Cephaloridine (δ-form); (2) the date after which the contents are not to be used; (3) the storage conditions.

Cephaloridine Injection

Category : Antibacterial.

Dose : Cephaloridine. By intramuscular injection, 1 to 4 g daily, in divided doses.

Usual strengths : 0.5 g; 1 g.

Standards : Cephaloridine Injection is a sterile solution of Cephaloridine in Water for Injection. It is prepared by dissolving the contents of a sealed container in the requisite amount of Water for Injection.

Content of cephaloridine, $C_{19}H_{17}N_3O_4S_2$: Determine the weight of the contents of each of ten containers as described in the test for **Uniformity of weight** under Injections. The weight of the contents of each container does not deviate from the weight stated on the label by more than 10 per cent except that in one container the weight may deviate by not more than 15 per cent.

Other requirements : Complies with the requirements stated under Injections.

The contents of the sealed container comply with the following requirements:

Description : White or almost white, crystalline powder; odour, slight, resembling that of pyridine.

Identification; Specific optical rotation; Light absorption; pH; Clarity of solution; Pyridine; Residual solvents; Pyrogens; Sterility; Undue toxicity; Sulphated ash; and Water : Comply with the requirements stated under Cephaloridine.

Assay : Carry out the **Assay** described under Cephaloridine, using the mixed contents of ten containers.

Storage : Store in light-resistant containers at a temperature not exceeding 15°. The constituted solution should be used within twenty-four hours when stored at a temperature not exceeding 20°.or within four days when stored in a cold place.

Labelling : The label on the sealed container states (1) the weight of Cephaloridine container in it; (2) whether the contents are Cephaloridine (α-form) or Cephaloridine (δ-form); (3) the date after which the contents are not intended to be used; (4) the storage conditions.

Cetostearyl Alcohol

Category : Pharmaceutical aid (ointment base).

Description : White, or cream-coloured unctuous mass, or almost white flakes or granules or cubes or castings; when heated, melts to a clear, colourless or pale-yellow liquid free from cloudiness or suspended matter; odour, faint and characteristic; taste, bland.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Solubility : Practically insoluble in *water*; less soluble in *alcohol* and in *light petroleum (boiling range, 40° to 60°)*; soluble in *solvent ether.*

Standards : Cetostearyl Alcohol is a mixture of solid aliphatic alcohols consisting chiefly of stearyl and cetyl alcohols.

Melting range : Between 45° and 53°, Appendix 5.11.

Acidity : Weigh accurately in a flask about 20 g and add 250 ml of *alcohol* previously neutralised to *phenolphthalein solution.* Heat on a water-bath and titrate the hot solution with *0.02N sodium hydroxide*, shaking vigorously and keeping the temperature as high as possible until a pink colour which persists for at least fifteen seconds is obtained; not more than 0.25 ml of *0.02N sodium hydroxide* is required for each g of the substance taken.

Iodine value : Not more than 3.0, Appendix 3.3.18.

Saponification value : Not more than 2.0, Appendix 3.3.20, using about 20 g.

Alcohols : To 3.5 g add 12 g of *stearic anhydride* and 10 ml of *xylene* and heat gently under a reflux condenser for thirty minutes. Cool, add in mixture of 40 ml of *pyridine* and 4 ml of *water*, reflux for a further thirty minutes, and titrate the hot solution with *N sodium hydroxide*, using *phenolphthalein solution* as indicator. Repeat the operation omitting the substance under examination; the difference between the titrations is not less then 12.8 ml and not more than 14.2 ml.

Hydrocarbons : Dissolve 2.0 g in 100 ml of *light petroleum (boiling range, 40° to 60°)*, warming slightly if necessary, and transfer the solution to a column, about 25 cm long and 1 cm in diameter, of *anhydrous alumina* which has been slurried with *light petroleum (boiling range, 40° to 60°).* Elute with two portions, each of 50 ml, of *light petroleum (boiling range, 40° to 60°)*, filter into a flask, remove the light petroleum and dry at 80°; the residue weighs not more than 30 mg.

Cetrimide

Category : Pharmaceutical aid (bactericide).

Description : White or creamy-white, voluminous, free-flowing powder; odour, faint and characteristic; taste, soapy and bitter.

Solubility : Freely soluble in *water*; soluble in *alcohol*; practically insoluble in *solvent ether.*

Standards : Cetrimide consists chiefly of tetradecyltrimethylammonium bromide together with smaller amounts of dodecyl- and hexadecyl-trimethylammonium bromides. It contains not less than 95.0 per cent of alkyltrimethylammonium bromides, calculated as $C_{17}H_{38}BrN$ with reference to the dried substance.

Identification : (A) To 10 ml of a 1 per cent w/v solution, add 2 ml of *potassium ferricyanide solution*; a yellow precipitate is produced.

(B) To 10 ml of a 1.0 per cent w/v solution, add 2 ml of a 10 per cent w/v solution of *sodium silicate*; a white flocculent precipitate is produced.

(C) To 10 ml of a 1.0 per cent w/v solution, add 2.0 ml of *dilute nitric acid*; a yellow precipitate is produced; filter and to the filtrate add 2 ml of *dilute nitric acid* and 1.0 ml of *silver nitrate solution*; a yellow precipitate is produced.

Clarity of solution : A 2.0 per cent w/v solution is not more than very slightly opalescent.

Acidity or Alkalinity : Dissolve 1 g in 50 ml of *water* and add two drops of *bromocresol purple solution.* Not more than 0.1 ml of either *0.1N hydrochloric acid* or *0.1N sodium hydroxide* is required to change the colour of the solution.

Amine salts : Carry out the **Assay** described below using a further 25.0 ml of the original solution and 10 ml of *0.1N hydrochloric acid* instead of the *0.1N sodium hydroxide.* The difference between the volume of *0.05M potassium iodate* required in this titration and that required in the assay is not more than 1.0 ml for each g of the substance used.

Sulphated ash : Not more than 0.5 per cent, Appendix 3.2.7.

Loss on drying : Not more than 2.0 per cent, determined on 1.0 g by drying in an oven at 105° for two hours, Appendix 5.8.

Assay : Weigh accurately 2.0 g and dissolve in sufficient *water* to produce 100.0 ml. Transfer 25.0 ml of the solution to a separator, add 25 ml of *chloroform*, 10 ml of *0.1N sodium hydroxide* and 10.0 ml of a freshly prepared 5.0 per cent w/v solution of *potassium iodide.* Shake well, allow to separate, and discard the chloroform layer. Shake the aqueous solution with three quantities, each of 10 ml, of *chloroform* and discard the chloroform solution. Add 40 ml of *hydrochloric acid*, allow to cool and titrate with *0.05M potassium iodate* until the deep brown colour is almost discharged. Add 2 ml of *chloroform* and continue the titration until the chloroform becomes colourless. Perform a blank determination on a mixture of 20 ml of *water*, 10.0 ml of the potassium iodide solution and 40 ml of *hydrochloric acid.* Each ml of *0.05M potassium iodate* is equivalent to 0.03364 g of $C_{17}H_{38}BrN$.

Storage : Store in well-closed containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Chloral Hydrate

$CCl_3CH(OH)_2$ Mol. Wt. 165.40

Category : Hypnotic and sedative.

Dose : 0.3 to 2.0 g.

Description : Colourless, transparent crystals; odour, pungent but not acrid; taste, pungent and slightly bitter. Volatilises slowly on exposure to air.

Solubility : Very soluble in *water*; freely soluble in *alcohol*, in *chloroform*, and in *solvent ether*.

Standards : Chloral Hydrate is 2,2,2-trichloroethane-1,1-diol. It contains not less than 99.5 per cent and not more than the equivalent of 102.5 per cent of $C_2H_3Cl_3O_2$.

Identification : (A) Take 2 ml of a 10.0 per cent w/v solution and add 1 ml of *sodium hydroxide solution*; chloroform separates. Acidify the supernatant aqueous solution with *acetic acid* and boil with *mercuric chloride solution*; a precipitate is produced.

(B) Heat with a few drops each of *aniline* and *sodium hydroxide solution*; phenyl isocyanide is produced. *(CAUTION – Poisonous).*

Clarity and colour of solution : A 10.0 per cent w/v solution is clear and colourless.

Acidity : To 2 ml of a 10.0 per cent w/v solution add a few drops of *dimethyl yellow solution*; the solution is coloured yellow or orange.

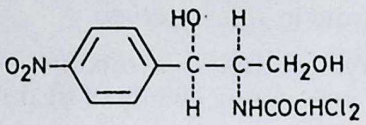
Chloral alcoholate : Warm 1 g with 6 ml of *water* and 0.5 ml of *sodium hydroxide solution*; filter, add sufficient *0.1N iodine* to impart a deep brown colour, and set aside for one hour; no yellow crystalline precipitate is produced and no smell of iodoform is perceptible.

Chloride : 3 g complies with the *limit test for chlorides*, Appendix 3.2.2.

Assay : Weigh accurately about 4 g and dissolve in 10 ml of *water* and add 30 ml of *N sodium hydroxide*. Allow the mixture to stand for two minutes, and then titrate with *N sulphuric acid*, using *phenolphthalein solution* as indicator. Titrate the neutralised liquid with *0.1N silver nitrate* using *potassium chromate solution* as indicator. Add two-fifteenth of the amount of *0.1N silver nitrate* used to the amount of *N sulphuric acid* used in the first titration and deduct the figure so obtained from the amount of *N sodium hydroxide* added. Each ml of *N sodium hydroxide*, obtained as difference, is equivalent to 0.1654 g of $C_2H_3Cl_3O_2$.

Storage : Store in tightly-closed, light resistant containers in a cool place.

Chloramphenicol



$C_{11}H_{12}Cl_2N_2O_5$ Mol. Wt. 323.13

Category : Antibacterial.

Dose : For an adult, 1.5 to 3 g daily, in divided doses; for a child, 25 to 50 mg per kg of body weight daily, in divided doses.

Description : Fine, white to greyish-white or yellowish-white, crystalline powder or crystals, needles or elongated plates; odourless; taste, very bitter.

Solubility : Slightly soluble in *water*; freely soluble in *alcohol* and in *acetone*; slightly soluble in *solvent ether*.

Standards : Chloramphenicol is 2,2-dichloro-*N*-[(1*R*, 2*R*)-2-hydroxy-α-hydroxymethyl-4-nitrophenethyl] acetamide. It contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of $C_{11}H_{12}Cl_2N_2O_5$, calculated with reference to the dried substance.

Identification : (A) Dissolve 10 mg in 1 ml of *alcohol (50 per cent)* and add 3 ml of a 1 per cent w/v solution of *calcium chloride*. Add 50 mg of *zinc powder* and heat on a water-bath for ten minutes. Decant the clear supernatant liquid into a test-tube, add 0.1 g of *anhydrous sodium acetate* and two drops of *benzoyl chloride*; shake for one minute and add 0.5 ml of a 10.5 per cent w/v solution of *ferric chloride hexahydrate* and if necessary, add sufficient *dilute hydrochloric acid* to produce a clear solution; a red-violet to purple colour is produced. Repeat the test with the same quantities of the same reagents in the same manner but omitting *zinc powder*; no colour is produced.

(B) To 5 ml of a 0.1 per cent w/v solution add a few drops of *silver nitrate solution*; no precipitate is produced.

(C) Heat 50 mg with 2 ml of *alcoholic potassium hydroxide solution* in a covered test-tube on a water-bath for fifteen minutes; the resulting solution gives the reactions of *chlorides*, Appendix 3.1.

(D) To 20 mg add 5 ml of *sodium hydroxide solution* and 2 ml of *pyridine*; shake well and heat in a water-bath; a brownish-red colour develops in the pyridine layer.

Melting range : Between 149° and 153°, Appendix 5.11.

Specific optical rotation : Between +17° and +20°, determined in a 5.0 per cent w/v solution in *ethyl alcohol*, Appendix 5.12.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

pH : Between 4.5 and 7.5, determined in a suspension prepared by shaking 50 mg with 10 ml of freshly boiled and cooled *water*, Appendix 5.10.

Chloride : Shake 50 mg with 10 ml of *water* and filter; to the filtrate add a few drops of *silver nitrate solution*; no opalescence is produced.

Undue toxicity : Complies with the test described under Bacitracin, using 0.5 ml of a solution containing 5 mg per ml in *saline solution* and applying sufficient heat to effect solution.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.125 g and dissolve in sufficient *water* to produce 250.0 ml. Dilute 10.0 ml with sufficient *water* to produce 250.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 278 nm, Appendix 5.15 A. Calculate the content of $C_{11}H_{12}Cl_2N_2O_5$ from the *extinction* obtained by repeating the assay on *chloramphenicol R.S.* and from the declared content of $C_{11}H_{12}Cl_2N_2O_5$ in the *chloramphenicol R.S.*

Chloramphenicol intended for parenteral administration complies with the following additional requirements:

Pyrogens : Complies with the *test for pyrogens*. Appendix 2.36, using 2 ml of a 0.25 per cent w/v solution in *water for injection* per kg of the rabbit's weight.

Histamine-like substances : Complies with the *test for histamine-like substances*, Appendix 2.35, using per kg of the body weight 0.6 ml of a solution containing 5 mg of chloramphenicol per ml.

Sterility : Complies with the *tests for sterility*, Appendix 4.6.

Storage : Store in tightly-closed, light-resistant containers. If the material is intended for parenteral preparations, the container should be sterile and sealed so as to exclude micro-organisms.

Labelling : The label on the container states (1) the date after which the contents are not intended to be used; (2) the storage conditions; (3) whether or not the contents are intended for parenteral administration.

Chloramphenicol Capsules

Category : Antibacterial.

Dose : Chloramphenicol. For an adult, 1.5 to 3.0 g daily, in divided doses; for a child, 25 to 50 mg per kg of body weight daily, in divided doses.

Usual strengths : 250 mg; 500 mg.

Standards : Chloramphenicol Capsules contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Chloramphenicol, $C_{11}H_{12}Cl_2N_2O_5$.

Identification; Melting range; Specific optical rotation : Suspend a quantity of the contents of the capsules equivalent to about 1.25 g of Chloramphenicol in 60 ml of *water* and extract with two quantities, each of 20 ml, of *light petroleum (boiling range, about 120°)*; wash the combined extracts with two quantities, each of 15 ml, of *water*, add the washings to the aqueous layer, extract with four quantities, each of 50 ml, of *solvent ether* and remove the ether from the combined extracts. The residue after drying to constant weight at 105°, complies with the tests for **Identification, Melting range** and **Specific optical rotation** described under Chloramphenicol.

Other requirements : Comply with the requirements stated under Capsules.

Assay : Weigh accurately a quantity of the mixed contents of 20 capsules equivalent to about 0.2 g of Chloramphenicol and dissolve in 800 ml of *water*, warming if necessary to effect solution, add sufficient *water* to produce 1000.0 ml. Dilute 10.0 ml of this solution to 100.0 ml with *water* and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 278 nm, Appendix 5.15 A. Calculate the content of $C_{11}H_{12}Cl_2N_2O_5$, taking 298 as the value of E(1 per cent, 1-cm) at the maximum at about 278 nm.

Storage : Store in tightly-closed containers.

Labelling : The label on the container states (1) the date after which the capsules are not intended to be used; (2) the storage conditions.

Chloramphenicol Eye Ointment

Category : Antibacterial.

Usual strength : 1 per cent w/w (10 mg per g).

Standards : Chloramphenicol Eye Ointment contains not less than 90.0 per cent and not more than 120.0 per cent of the stated amount of Chloramphenicol, $C_{11}H_{12}Cl_2N_2O_5$.

Identification : Heat a quantity of the ointment equivalent to about 20 mg of Chloramphenicol with 20 ml of *methyl alcohol* for twenty minutes. Cool in ice, filter and carefully evaporate to dryness on a water-bath; dissolve the residue in 5 ml of *sodium hydroxide solution* and

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

2 ml of *pyridine*, shake well, and heat in a water-bath; a brownish-red colour is produced.

Other requirements : Complies with the requirements stated under Eye Ointments.

Assay : Use either of the following methods; however, the results obtained from the microbiological assay shall be official.

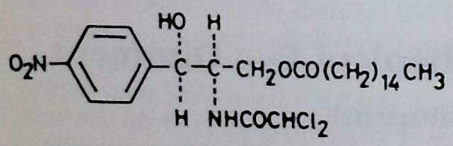
(1) Weigh accurately a quantity equivalent to about 10 mg of Chloramphenicol, dissolve in 50 ml of *light petroleum (boiling range, 40° to 60°)* and extract with three successive quantities, each of 50 ml, of *water*, combine the extracts, dilute to 200.0 ml with *water* and mix well. Filter, discarding the first 20 ml of the filtrate, and dilute 10.0 ml of the filtrate to 50.0 ml with *water*. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 278 nm, Appendix 5.15 A. Calculate the content of $C_{11}H_{12}Cl_2N_2O_5$, taking 298 as the value of E(1 per cent, 1-cm) at 278 nm.

(2) Weigh accurately about 1 g, transfer to a separator, add 50 ml of *light petroleum (boiling range, 40° to 60°)* and shake well. Extract with four successive quantities, each of 20 ml, of buffer solution No. 1, Appendix 4.1, Table 2. Combine the extracts and dilute to a suitable volume with buffer solution No. 1 to produce a solution containing 2.5 µg per ml, of chloramphenicol. Carry out the *microbiological assay of antibiotics, Method B*, Appendix 4.1. Express the result in mg of chloramphenicol per g.

Storage : Store in a cool place.

Labelling : The label on the container states (1) the date after which the contents are not intended to be used; (2) the storage conditions.

Chloramphenicol Palmitate



$C_{27}H_{42}Cl_2N_2O_6$ Mol. Wt. 561.54

Category : Antibacterial.

Dose : For an adult, the equivalent of 1.5 to 3 g of chloramphenicol daily, in divided doses; for a child, the equivalent of 25 to 50 mg of chloramphenicol per kg of body weight daily, in divided doses.

174 mg of Chloramphenicol Palmitate is equivalent to 100 mg of Chloramphenicol.

Description : Fine, white or greyish-white unctuous powder; odour, faint; taste, bland.

Solubility : Practically insoluble in *water*; slightly soluble in *alcohol*; soluble in *acetone*, in *chloroform* and in *solvent ether*.

Standards : Chloramphenicol Palmitate is (*2R*, *3R*)-2-dichloroacetamido-3-hydroxy-3-(4-nitrophenyl)-propyl palmitate. It contains not less than 97.0 per cent and not more than the equivalent of 103.0 per cent of $C_{27}H_{42}Cl_2N_2O_6$, calculated with reference to the dried substance.

Identification : (A) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.003 per cent w/v solution in *alcohol* exhibits a maximum only at about 271 nm; *extinction* at this maximum, about 0.53, Appendix 5.15 A.

(B) Dissolve 10 mg in 4 ml of *alcohol*, add 1 ml of *2N sulphuric acid* and 50 mg of *zinc powder*, and allow to stand for ten minutes. Filter, cool the filtrate in ice and add 0.5 ml of *sodium nitrite solution* and, after two minutes, 1 g of *urea*, followed by 1 ml of *β-naphthol solution* and 2 ml of *10N sodium hydroxide*; a red colour develops. Repeat the test omitting the zinc powder; no red colour is produced.

(C) To 50 mg add 2 ml of *alcoholic potassium hydroxide solution* and heat on a water-bath for 15 minutes; the solution gives the reactions of *chlorides*, Appendix 3.1.

Melting range : Between 87° and 95°, Appendix 5.11.

Specific optical rotation : Between +21° and +25°, determined in a 5.0 per cent w/v solution in *ethyl alcohol*, Appendix 5.12.

Free chloramphenicol : Not more than 450 parts per million, determined by the following method: Dissolve with the aid of gentle heat, 1.0 g in 80 ml of *xylene*, cool and extract with three successive quantities, each of 15 ml, of *water*; discard the *xylene*, and dilute the combined aqueous extracts to 50 ml with *water*; extract the solution with 10 ml of *carbon tetrachloride*, allow to separate, discard the carbon tetrachloride, centrifuge a portion of the aqueous solution, and measure the *extinction* of a 1-cm layer of the clear aqueous solution at the maximum at about 278 nm, using as the blank a solution prepared by repeating the procedure without the sample; the *extinction* of this blank solution must not be greater than 0.05, Appendix 5.15 A.

Calculate the content of free chloramphenicol, taking 298 as the value of E(1 per cent, 1-cm) at the maximum at about 278 nm.

Free acid : Dissolve 1.0 g by warming to 35° in 5 ml of a mixture of equal volumes of *alcohol* and *solvent ether*, previously neutralised to *phenolphthalein solution*. Titrate with *0.1N sodium hydroxide* using a few drops of

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

phenolphthalein solution as indicator until a pink colour persisting for 30 seconds is obtained. Not more than 0.8 ml of *0.1N sodium hydroxide* is required.

Undue toxicity : Complies with the test described under Bacitracin, using 1 ml of a suspension of 60 mg in a 10 per cent w/v solution of *acacia* and administering orally by means of a canula or other suitable device.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying "in vacuo", Appendix 5.8.

Assay : Weigh accurately about 60 mg and dissolve in sufficient *ethyl alcohol* to produce 100.0 ml. Dilute 10.0 ml of this solution to 200.0 ml with *ethyl alcohol* and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 271 nm, Appendix 5.15 A. Calculate the content of $C_{27}H_{42}Cl_2N_2O_6$, taking 178 as the value of E(1 per cent, 1-cm) at the maximum at about 271 nm.

Storage : Store in tightly-closed, light-resistant containers.

Labelling : The label on the container states (1) the date after which the contents are not intended to be used; (2) the storage conditions.

Chloramphenicol Palmitate Oral Suspension

Chloramphenicol Mixture

Category : Antibacterial.

Dose : For an adult, the equivalent of 1.5 to 3 g of chloramphenicol daily, in divided doses; for a child, the equivalent of 25 to 50 mg of chloramphenicol per kg of body weight in divided doses.

Usual strength : 125 mg of chloramphenicol in 5 ml.

Standards : Chloramphenicol Palmitate Oral Suspension contains a quantity of Chloramphenicol Palmitate equivalent to not less than 95.0 per cent and not more than 115.0 per cent of the stated amount of chloramphenicol, $C_{11}H_{12}Cl_2N_2O_5$.

Identification : Extract a quantity of the suspension equivalent to about 7.5 mg of chloramphenicol with 10 ml of *chloroform* and carefully evaporate the clear chloroform solution on a water-bath to dryness. Dissolve the residue in 250 ml of *alcohol*. The light absorption, in the range 230 to 350 nm, of a 1-cm layer of the resulting solution exhibits a maximum only at about 271 nm and a minimum only at about 234 nm, Appendix 5.15 A.

pH : Between 4.5 and 7.0, Appendix 5.10.

Polymorph A : To a volume of the mixture equivalent to 125 mg of chloramphenicol add 35 ml of *water*, mix, centrifuge for forty minutes at not less than 18,000 revolutions per minute and discard the supernatant liquid. Wash the residue by adding 2 ml of *water*, triturating to form a paste, adding 18 ml of *water*, mixing thoroughly, centrifuging and discarding the supernatant liquid. Wash the residue twice more in a similar manner, dry at 20° for sixteen hours at a pressure not exceeding 5 torr and grind to a fine powder. Prepare a mull of the residue by triturating a small quantity with about twice its weight of liquid paraffin until a smooth creamy paste is obtained, compress a portion of the mull between rock salt plates and record the *infra-red absorption spectrum*, Appendix 5.15 B, over the range 770 cm^{-1} to 910 cm^{-1} using conditions such that between 20 and 30 per cent transmittance occurs at 810 cm^{-1}. Repeat the operation using a mull prepared with a standard mixture obtained by mixing thoroughly together 1 part by weight of *chloramphenicol palmitate (polymorph A) R.S.* and 9 parts by weight of *chloramphenicol palmitate R.S.* On each of the spectra, draw a straight base line between the minima occurring at about 880 cm^{-1} and 790 cm^{-1} and using these base lines measure the heights of the peaks occurring at the maxima at about 858 cm^{-1} and 840 cm^{-1}. In the spectrum obtained with the preparation being examined, the ratio of the peak height at about 858 cm^{-1} to that at the maximum at about 840 cm^{-1} is greater than the corresponding ratio in the spectrum obtained with the standard mixture.

Assay : Weigh accurately a quantity of the suspension equivalent to about 125 mg of chloramphenicol, add 10 ml of *water* and shake with four quantities, each of 20 ml, of *chloroform*, filtering each extract through cottonwool, previously washed with *chloroform*, into a 100-ml volumetric flask. Dilute to volume with *chloroform* and mix well. Dilute 2.0 ml of the solution to 100.0 ml with *alcohol* and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 271 nm using 1 ml of *chloroform* diluted to 50 ml with *alcohol* as blank, Appendix 5.15 A

Determine the weight per ml of the suspension and calculate the content of chloramphenicol w/v taking 178 as the value of E(1 per cent, 1-cm) at the maximum at about 271 nm and a factor of 0.575 (for the conversion of the content of chloramphenicol palmitate to chloramphenicol).

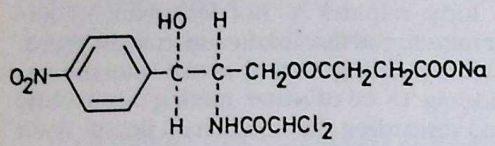
Storage : Store in tightly-closed, light-resistant containers.

Labelling : The label on the container states (1) the strength in terms of the equivalent amount of chloramphenicol; (2) the date after which the contents are not intended to be used; (3) the storage conditions.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Chloramphenicol Sodium Succinate



$C_{15}H_{15}Cl_2N_2NaO_8$ Mol. Wt. 445.19

Category : Antibacterial.

Dose : By intravenous injection, the equivalent of 3 to 4 g of chloramphenicol daily, in divided doses.

NOTE – 140 mg of Chloramphenicol Sodium Succinate is approximately equivalent to 100 mg of chloramphenicol.

Description : White or yellowish-white powder; hygroscopic.

Solubility : Freely soluble in *water* and in *alcohol*; practically insoluble in *chloroform* and in *solvent ether.*

Standards : Chloramphenicol Sodium Succinate is sodium (2*R*, 3*R*)-2-dichloroacetamido-3-hydroxy-3-(4-nitrophenyl) propyl succinate. It contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of $C_{15}H_{15}Cl_2N_2NaO_8$, calculated with reference to the anhydrous substance.

Identification : (A) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.002 per cent w/v solution exhibits a maximum only at 276 nm; *extinction* at 276 nm, about 0.43, Appendix 5.15 A.

(B) Dissolve 10 mg in 2 ml of *alcohol*, add 4.5 ml of *dilute sulphuric acid* and 50 mg of *zinc powder*, allow to stand for 10 minutes and decant the supernatant liquid or filter, if necessary. Cool the resulting solution in ice and add 0.5 ml of *sodium nitrite solution* and after 2 minutes 1 g of *urea* followed by 1 ml of *β-naphthol solution* and 2 ml of *sodium hydroxide solution*; a red colour develops. Repeat the test omitting the zinc powder; no red colour is produced.

(C) To 5 ml of a 0.1 per cent w/v solution add a few drops of *silver nitrate solution*; no precipitate is produced. Heat 50 mg with 2 ml of *alcoholic potassium hydroxide solution* on a water-bath for fifteen minutes, add 50 mg of *decolourising charcoal*, shake and filter. The filtrate when treated with *silver nitrate solution*, yields a curdy precipitate which is insoluble in *nitric acid*, but soluble, after being well washed with *water*; in *dilute ammonia solution* from which it is reprecipitated by the addition of *nitric acid.*

(D) A solution (1 in 20) gives the reactions of *sodium*, Appendix 3.1.

Specific optical rotation : Between +5.0° and +8.0° determined in a 5 per cent w/v solution, Appendix 5.12.

pH : Between 6.0 and 7.0, determined in a 25 per cent w/v solution, Appendix 5.10.

Chloramphenicol : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel GF 254* as the coating substance and as the mobile phase, a mixture of 9 volumes of *chloroform*, 1 volume of *methyl alcohol*, and 0.1 volume of *water.* Apply separately to the plate 10 µl of each of two solutions in *acetone* containing (1) 1 per cent w/v of the substance being examined and (2) 0.02 per cent w/v of *chloramphenicol R.S.* After removal of the plate allow it to dry in air and examine under an ultra-violet lamp having a maximum output at about 254 nm. The spot in the chromatogram obtained with solution (2) is more intense than any corresponding spot in the chromatogram obtained with solution (1).

Undue toxicity : Complies with the test described under Bacitracin, using 0.5 ml of a solution containing the equivalent of 5 mg chloramphenicol per ml in *saline solution.*

Water : Not more than 5.0 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately about 0.2 g and dissolve in sufficient *water* to produce 500.0 ml; dilute 5.0 ml of this solution to 100.0 ml with *water* and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 276 nm, Appendix 5.15 A. Calculate the content of $C_{15}H_{15}Cl_2N_2NaO_8$, taking 216 as the value of E(1 per cent 1-cm) at the maximum at about 276 nm.

Chloramphenicol Sodium Succinate intended for parenteral administration complies with the following additional requirements:

Histamine-like substances : Complies with the test for *histamine-like substances*, Appendix 2.35, using a dose containing the equivalent of 5.0 mg chloramphenicol per ml.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using 1 ml per kg of the rabbits's weight of a solution in *water for injection* containing the equivalent of 5 mg of chloramphenicol in each ml.

Sterility : Complies with the *tests for sterility*, Appendix 4.6.

Storage : Store in tightly-closed and light-resistant containers. If it is intended for parenteral administration, the container should be sterile and sealed so as to exclude micro-organisms.

Labelling : The label on the container states (1) the date after which the contents are not intended to be used; (2) the storage conditions; (3) whether or not the contents are intended for parenteral administration.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Chloramphenicol Sodium Succinate Injection

Category : Antibacterial; antirickettsial.

Dose : By intravenous injection, the equivalent of 3 to 4 g of chloramphenicol daily, in divided doses.

Usual strength : The equivalent of 1 g of chloramphenicol.

Standards : Chloramphenicol Sodium Succinate Injection is a sterile solution of Chloramphenicol Sodium Succinate in Water for Injection. It is prepared by dissolving the contents of a sealed container in the requisite amount of Water for Injection.

Content of chloramphenicol, $C_{11}H_{12}Cl_2N_2O_5$: Determine the weight of the contents of each of ten containers as described in the test of **Uniformity of weight** under Injections. From the result of the assay calculate the proportionate amount of chloramphenicol, $C_{11}H_{12}Cl_2N_2O_5$ in each container; each g of chloramphenicol sodium succinate, $C_{15}H_{15}Cl_2N_2NaO_8$ is equivalent to 0.7257 g of chloramphenicol, $C_{11}H_{12}Cl_2N_2O_5$. This amount does not deviate from the amount stated on the label by a greater percentage than that shown in column A of the Table of Deviations, except that in one container the amount may deviate by not more than twice the percentage shown.

Other requirements : Complies with the requirements stated under Injections.

The contents of the sealed container comply with the following requirements:

Description : White or yellowish-white powder.

Identification; Specific optical rotation; pH; Chloramphenicol; Undue toxicity; Histamine-like substances; Pyrogens; Sterility and Water : Comply with the requirements stated under Chloramphenicol Sodium Succinate.

Assay : Carry out the **Assay** described under Chloramphenicol Sodium Succinate, using 0.2 g of the mixed contents of ten containers.

Storage : Store in light-resistant containers. The constituted solution should be used within twenty-four hours of preparation.

Labelling : The label on the container states (1) the quantity of Chloramphenicol Sodium Succinate contained in it in terms of the equivalent amount of chloramphenicol; (2) the date after which the contents are not intended to be used; (3) the storage conditions.

Chlorbutol

Chlorbutanol

$CCl_3.C(CH_3)_2\ OH, \frac{1}{2}\ H_2O$ Mol. Wt. 186.48

Category : Pharmaceutical aid (antimicrobial preservative).

Description : Colourless to white crystals; odour and taste, characteristic, musty, and somewhat camphoraceous.

Solubility : Slightly soluble in *water*; freely soluble in *alcohol*, in *solvent ether*, in *chloroform* and in volatile oils.

Standards : Chlorbutol is the hemihydrate of 1,1,1-trichloro-2-methylpropan-2-ol. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_4H_7Cl_3O$, calculated with reference to the anhydrous substance.

Identification : (A) Take 5 ml of a freshly prepared 0.5 per cent w/v solution and add 1 ml of a 4 per cent w/v solution of *sodium hydroxide* followed slowly by the addition of 2 ml of *iodine solution*; a yellow precipitate of iodoform is produced.

(B) Take 0.1 g and add 4 ml of *N sodium hydroxide*, mix thoroughly, and add a few drops of *aniline*; phenyl isocyanide is produced.

Melting range : Not lower than 77°, determined without previous drying, Appendix 5.11.

Acidity : Dissolve 2 g in 20 ml of *methyl alcohol*, add 0.1 ml of *bromothymol blue solution* and titrate with *0.1N sodium hydroxide*; not more than 0.1 ml of *0.1N sodium hydroxide* is required.

Chloride : 0.5 g, dissolved in 10 ml of *alcohol*, complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Water : Not less than 0.1 per cent and not more than 6.0 per cent w/w, Appendix 3.3.25.

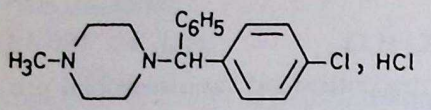
Assay : Weigh accurately about 0.2 g and dissolve in 5 ml of *alcohol*. Add 5 ml of *sodium hydroxide solution*, and boil under a reflux condenser for fifteen minutes. Cool, dilute with 20 ml of *water*, add 5 ml of *nitric acid*, 1 ml of *nitrobenzene*, and 50.0 ml of *0.1N silver nitrate*, and shake vigorously for one minute. Add 4 ml of *ferric ammonium sulphate solution* and titrate the excess of silver nitrate with *0.1N ammonium thiocyanate*. Each ml of *0.1N silver nitrate* is equivalent to 0.005917 g of $C_4H_7Cl_3O$.

Storage : Store in tightly-closed containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Chlorcyclizine Hydrochloride



$C_{18}H_{21}ClN_2, HCl$ Mol. Wt. 337.29

Category : Antihistaminic.

Dose : 50 to 200 mg daily, in divided doses.

Description : White, crystalline powder; odourless or almost odourless; taste, bitter.

Solubility : Freely soluble in *water* and in *chloroform*; soluble in *alcohol*; almost insoluble in *solvent ether*.

Standards : Chlorcyclizine Hydrochloride is 1-(4-chlorobenzhydryl)-4-methylpiperazine hydrochloride. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_{18}H_{21}ClN_2, HCl$, calculated with reference to the dried substance.

Identification : (A) The light absorption, in the range 225 to 350 nm, of a 1-cm layer of a 0.001 per cent w/v solution in *alcohol* exhibits a maximum only at 230 nm; *extinction* at 230 nm, about 0.44, Appendix 5.15 A.

(B) Dissolve 25 mg in 5 ml of *sulphuric acid*; a brilliant yellow colour is produced, which disappears when this solution is poured into 20 ml of *water*, leaving a colourless solution.

(C) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

pH : Between 5.0 and 6.0, determined in a 1.0 per cent w/v solution, Appendix 5.10.

N-methylpiperazine : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 90 volumes of *chloroform*, 8 volumes of *methyl alcohol*, and 2 volumes of *strong ammonia solution* as the mobile phase. Apply separately to the plate 20 µl of each of two solutions freshly prepared in *methyl alcohol* containing (1) 1.0 per cent w/v of the substance being examined and (2) 0.005 per cent w/v of *N-methylpiperazine R.S.* After removal of the plate, allow it to dry in air, heat at 110° for fifteen minutes, and spray with a mixture of one volume of a 10 per cent w/v solution of *platinic chloride* and 50 volumes of a 2 per cent w/v solution of *potassium iodide*. The spot in the chromatogram obtained with solution (2) is more intense than any corresponding spot in the chromatogram obtained with solution (1).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 2.5 per cent, determined on 1.0 g by drying in an oven at 120° for three hours, Appendix 5.8.

Assay : Weigh accurately about 0.5 g and dissolve in 50 ml of *glacial acetic acid*. Add 10 ml of *mercuric acetate solution* and titrate with *0.1N perchloric acid*, determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.01686 g of $C_{18}H_{21}ClN_2, HCl$.

Storage : Store in well-closed, light-resistant containers.

Chlorcyclizine Tablets

Category : Antihistaminic.

Dose : Chlorcyclizine Hydrochloride, 50 to 200 mg daily, in divided doses.

Usual strength : 50 mg.

Standards : Chlorcyclizine Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Chlorcyclizine Hydrochloride, $C_{18}H_{21}ClN_2, HCl$. The tablets may be coated.

Identification : Extract a quantity of the powdered tablets equivalent to about 0.25 g of Chlorcyclizine Hydrochloride with two quantities, each of 10 ml, of *chloroform*, combine the extracts, filter, and evaporate to dryness. The residue complies with **Identification** tests (B) and (C) described under Chlorcyclizine Hydrochloride.

Disintegration : Maximum time, fifteen minutes, Appendix 5.6.1.

Other requirements : Comply with the requirements stated under Tablets.

N-methylpiperazine : Comply with the test described under Chlorcyclizine Hydrochloride, using as solution (1) a solution prepared by triturating a quantity of the powdered tablets equivalent to 0.1 g of Chlorcyclizine Hydrochloride with 10 ml of *methyl alcohol* and filtering.

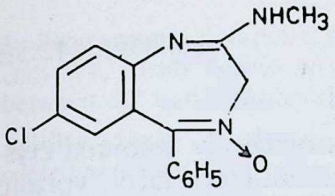
Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powdered tablets equivalent to about 0.1 g of Chlorcyclizine Hydrochloride, add 75 ml of *0.1N sulphuric acid* and shake for thirty minutes. Dilute to 200.0 ml with *0.1N sulphuric acid*, filter, dilute 50.0 ml of the filtrate to 100.0 ml with *0.1N sulphuric acid* and dilute 5.0 ml of dilution to 100.0 ml with *0.1N sulphuric acid*. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 231 nm, Appendix 5.15 A. Calculate the content of $C_{18}H_{21}ClN_2, HCl$, taking 512 as the value of E(1 per cent, 1-cm) at the maximum at about 231 nm.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Storage : Store in tightly-closed, light-resistant containers.

Chlordiazepoxide



$C_{16}H_{14}ClN_3O$ Mol. Wt. 299.76

Category : Tranquilliser.

Dose : 10 to 100 mg daily, in divided doses.

Description : Yellow crystalline powder; practically odourless.

Solubility : Sparingly soluble in *chloroform* and in *alcohol*; insoluble in *water*.

Standards : Chlordiazepoxide is 7-chloro-2-methylamino-5-phenyl-3*H*-1, 4-benzodiazepine-4-oxide. It contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of $C_{16}H_{14}ClN_3O$, calculated with reference to the dried substance.

Identification : (A) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.0005 per cent w/v solution in *0.1N hydrochloric acid* exhibits two maxima at 246 nm and 308 nm; *extinction* at 246 nm, about 0.56 and at 308 nm, about 0.16, Appendix 5.15 A.

(B) Dissolve 0.2 g in 4 ml of hot *dilute hydrochloric acid*, heat at 100°C for ten minutes, cool, and filter; 2 ml of the filtrate gives the reactions of *primary aromatic amines*, Appendix 3.1.

Melting range : Between 240° and 244°, Appendix 5.11.

Decomposition products : Carry out in subdued light the method for *thin-layer chromatography*, Appendix 5.4.3, using a suitable silica gel as the coating substance and a mixture of 1 volume of *alcohol* and 24 volumes of *ethyl acetate* as the mobile phase, but allowing the solvent front to travel 12 cm beyond the line of application. Apply separately to the plate, ensuring that the diameters of the spots do not exceed 6 mm, 10 µl of each of three freshly prepared solutions in *acetone*, containing (1) 2.0 per cent w/v of the substance being examined; (2) 0.002 per cent w/v of *7-chloro-1,3-dihydro-5-phenyl-1,4-benzodiazepine-2-one-4-oxide R.S.*; (3) 0.001 per cent w/v of *2-amino-5-chlorobenzophenone R.S.*

After removal of the plate, allow it to dry in air until the odour of the solvent is no longer detectable. Spray the plate lightly with a 10 per cent w/v solution of *sulphuric acid* in *alcohol*, heat at 105° for thirty minutes, and spray in succession with a 0.1 per cent w/v solution of *sodium nitrite*, 0.5 per cent w/v solution of *ammonium sulphamate* and 0.1 per cent w/v solution of *N-(1-naphthyl)ethylenediamine hydrochloride* in *alcohol*. Any spots formed in the chromatogram obtained with solution (1) are not greater in intensity than the corresponding spots in the chromatogram obtained with solutions (2) and (3).

Heavy metals : Not more than 20 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

Sulphated ash : Not more than 0.1 per cent Appendix 3.2.7.

Loss on drying : Not more than 0.3 per cent, determined on 1.0 g by drying in an oven at 105° for three hours; Appendix 5.8.

Assay : Weigh accurately about 0.8 g and dissolve in 90 ml of *chloroform*, add three drops of *alcoholic methyl red solution* and titrate with *0.1N perchloric acid in dioxan* to a pink end-point. Carry out a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02998 g of $C_{16}H_{14}ClN_3O$.

Storage : Store in tightly-closed, light-resistant containers.

Chlordiazepoxide Tablets

Category : Tranquilliser.

Dose : Chlordiazepoxide, 10 to 100 mg daily, in divided doses.

Usual strengths : 5 mg; 10 mg.

Standards : Chlordiazepoxide Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Chlordiazepoxide, $C_{16}H_{14}ClN_3O$. The Tablets may be coated.

Identification : (A) Dilute 1 ml of the final solution obtained in the **Assay** to 4 ml with *0.1N hydrochloric acid*. The light absorption, in the range 230 to 350 nm, of a 1-cm layer of the resulting solution exhibits two maxima, at 246 nm and at 308 nm, Appendix 5.15 A.

(B) To a quantity of the powdered tablets equivalent to 0.2 g of Chlordiazepoxide add 4 ml of hot *2N hydrochloric acid*, heat at 100° for ten minutes, cool and filter; 2 ml of the filtrate gives the reactions of *primary aromatic amines*, Appendix 3.1.

Decomposition products : Comply with the test

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

described under Chlordiazepoxide. For solution (1) shake a quantity of the powdered tablets equivalent to 0.1 g of Chlordiazepoxide with 10 ml of *acetone* and allow to settle and decant the clear supernatant liquid. Solution (2) contains 0.03 per cent w/v of *7-chloro-1, 3-dihydro-5-phenyl-1, 4-benzodiazepin-2-one-4-oxide R.S.* in *acetone*. Solution (3) contains 0.001 per cent w/v of *2-amino-5-chlorobenzophenone R.S.* in *acetone*. Apply 10 µl of solutions (1) and (3) and also separately 1 µl of solutions (1) and (2).

Any spot in the chromatogram obtained with 10 µl of solution (1) except that corresponding to 7-chloro-1, 3-dihydro-5-phenyl-1, 4-benzodiazepin-2-one-4-oxide is not more intense than the spot yielded by 2-amino-5-chlorobenzophenone in the chromatogram obtained with 10 µl of solution (3); the spot yielded by 7-chloro-1, 3-dihydro-5-phenyl-1, 4-benzodiazepin-2-one-4-oxide in the chromatogram obtained with 1 µl of solution (3) is more intense than any corresponding spot in the chromatogram obtained with 1 µl of solution (1)

Uniformity of content : Powder one tablet, shake with 50 ml of *0.1N hydrochloric acid* for twenty minutes and add sufficient *0.1N hydrochloric acid* to produce 100.0 ml. Filter and dilute a suitable quantity of the filtrate containing the equivalent of 0.8 mg of Chlordiazepoxide with sufficient *0.1N hydrochloric acid* to produce 50.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 308 nm, Appendix 5.15 A. Calculate the content of $C_{16}H_{14}ClN_3O$, taking 327 as the value of E(1 per cent, 1-cm) at the maximum at about 308 nm.

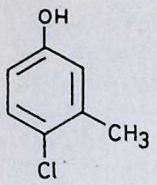
Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 90 and 110 per cent of the average except that for one tablet the content may be between 85 and 115 per cent of the average.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 20 mg of Chlordiazepoxide and shake with 150 ml of *0.1N hydrochloric acid* for twenty minutes. Add sufficient *0.1N hydrochloric acid* to produce 250.0 ml and filter. Dilute 10.0 ml of the filtrate to 50.0 ml with *0.1N hydrochloric acid* and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 308 nm, Appendix 5.15 A. Calculate the content of $C_{16}H_{14}ClN_3O$, taking 327 as the value of E(1 per cent, 1-cm) at the maximum at about 308 nm.

Storage : Store in light-resistant containers.

Chlorocresol



C_7H_7ClO Mol. Wt. 142.58

Category : Bacteriostatic.

Description : Colourless or faintly coloured crystals; odour, characteristic; and not tarry; volatile in steam.

Solubility : Slightly soluble in *water*; soluble in hot *water*; readily soluble in *alcohol* and in *solvent ether*.

Standards : Chlorocresol is 4-chloro-3-methyl-phenol.

Identification : (A) To a saturated solution in *water* add one drop of *ferric chloride test-solution*, a bluish colour is produced.

(B) To 50 mg add 0.5 g of a *anhydrous sodium carbonate*, mix and ignite strongly, cool, and add 5 ml of *water* and boil. Cool, acidify with *nitric acid*, filter and add *silver nitrate solution*; a white precipitate is produced.

Melting range : Between 64° and 66°, Appendix 5.11.

Non-volatile matter : Not more than 0.1 per cent, determined on 1.0 g by volatilising on a water-bath and drying at 105°.

Storage : Store in tightly-closed containers.

Chloroform

$CHCl_3$ Mol. Wt. 119.38

Category : General anaesthetic; pharmaceutical aid (solvent and preservative).

Description : Colourless, volatile liquid; odour, characteristic; taste, sweet and burning.

Solubility : Slightly soluble in *water*; freely miscible with *ethyl alcohol* and with *solvent ether*.

Standards : Chloroform is trichloromethane to which 1 to 2 per cent v/v of ethyl alcohol has been added.

Identification : (A) It is not inflammable. The vapour

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

introduced into a Bunsen flame produces a green colour and gives rise to noxious vapours having a characteristic odour.

(B) Warm one drop with one drop of *aniline* and 1 ml of *sodium hydroxide solution*; the characteristic odour of phenyl isocyanide is produced.

Wt. per ml : Between 1.474 and 1.478 g, Appendix 5.19.

Boiling range : A variable fraction, not exceeding 5 per cent v/v, distils below 60° and the remainder distils between 60° to 62°, Appendix 5.3.

Acidity : Shake 10 ml with 20 ml of freshly boiled and cooled *water* for three minutes, and allow to separate. To a 5-ml portion of the aqueous layer add 0.1 ml of *litmus solution*; the colour produced is not different from that produced on adding 0.1 ml of *litmus solution* to 5 ml of freshly boiled and cooled *water*.

Chloride : To another 5-ml portion of the aqueous layer obtained in the test for **Acidity**, add 5 ml of *water* and 0.2 ml of *silver nitrate solution*; no opalescence is produced.

Free chlorine : To another 10-ml portion of the aqueous layer, obtained in the test for **Acidity** add 1 ml of *cadmium iodide solution* and two drops of *starch solution*; no blue colour is produced.

Aldehyde : Shake 5 ml with 5 ml of *water* and 0.2 ml of *alkaline potassium mercuri-iodide solution* in a stoppered bottle and set aside in the dark for fifteen minutes; no more than a pale yellow colour is produced.

Decomposition products : Place 20 ml of the chloroform in a glass-stoppered vessel, previously mixed with *sulphuric acid*, add 15 ml of *sulphuric acid* and four drops of *formaldehyde solution*, shake the mixture frequently during half an hour and set aside for further half an hour, the vessel being protected from light during the test; the acid layer is not more than slightly coloured.

Foreign organic matter : Shake 20 ml with 10 ml of *sulphuric acid* in a stoppered vessel previously rinsed with *sulphuric acid* for five minutes and set aside in the dark for thirty minutes, both the acid and chloroform layers remain colourless. To 2 ml of the acid layer add 5 ml of *water*; the liquid remains colourless and clear, and has no unpleasant odour. Add a further 10 ml of *water* and 0.2 ml of *silver nitrate solution*; no opalescence is produced.

Foreign chlorine compounds : Shake 15 ml of the chloroform layer obtained in the test for foreign organic matter with 30 ml of *water* in a stoppered bottle for three minutes, and allow separation to take place; to the aqueous layer add 0.2 ml of *silver nitrate solution* and set aside in the dark for five minutes; no opalescence is produced.

Foreign odour : Allow 10 ml to evaporate from a large piece of filter paper placed on a warm plate; no foreign odour is detectable at any stage of the evaporation.

Non-volatile matter : Not more than 0.004 per cent w/v, determined on 25 ml by evaporation and drying at 105°.

Storage : Store in tightly-closed, glass-stoppered, light-resistant bottles.

NOTE – Care should be taken not to vaporise chloroform in the presence of a flame because of the production of harmful gases.

Chloroform Spirit

Category : Pharmaceutical aid (flavouring and preservative).

Description : Colourless, volatile liquid; odour, characteristic; teste, sweet and burning.

Standards : Chloroform Spirit is a 5.0 per cent v/v solution of Chloroform in Alcohol.

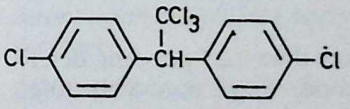
Alcohol content : Between 83 and 87 per cent v/v, Appendix 5.2 A.

Wt. per ml : Between 0.856 and 0.862 g, determined at 20°, Appendix 5.19.

Storage : Store in tightly-closed, light-resistant, glass-stoppered containers.

Chlorophenothane

Dicophane, DDT



$C_{14}H_9Cl_5$ Mol. Wt. 354.49

Category : Pediculicide (arthropod toxicant).

Description : White or nearly white crystals, powder, flakes, or small granules; odourless, or has a slight, aromatic odour.

Solubility : Insoluble in *water*; sparingly soluble in *alcohol* and freely soluble in boiling *alcohol*; freely soluble in *acetone*, in *chloroform* and in *solvent ether*.

Standards : Chlorophenothane is a mixture consisting chiefly of 1, 1, 1-trichloro-2, 2-bis-(4-chlorophenyl) ethane and varying amounts of an isomer and the carbinol resulting from condensation of one molecular proportion of chlorobenzene with chloral hydrate. It contains the equivalent of not less

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

than 95.0 per cent and not more than 102.0 per cent of $C_{14}H_9Cl_5$.

Identification : (A) Dissolve 0.2 g by heating in a test-tube with 10 ml of *alcohol* to boiling; add 0.5 ml of *N potassium hydroxide* and 3.5 ml of *water*, mix, cool and scratch the inner surface of the test-tube with a glass rod. Collect the crystals formed on a small filter, wash with a few ml of *dilute alcohol* and dry; the crystals melt at about 90°, Appendix 5.11.

(B) Heat a small quantity with a 0.5 per cent w/v solution of *hydroquinone* in *nitrogen-free sulphuric acid*; a wine-red colour is produced.

Congealing temperature : Not lower than 89°, Appendix 5.5.

Acidity : Dissolve 10.0 g in 25 ml of *acetone*, warming if necessary, add 75 ml of *water*, and titrate immediately with *0.1N sodium hydroxide*, using *methyl red solution* as indicator. Repeat the operation without the substance being examined; the difference between the titrations does not exceed 6.0 ml.

Hydrolysable chlorine : Between 9.5 per cent and 11.5 per cent, determined by the following method: Weigh accurately about 0.5 g, add 40 ml of *0.5N alcoholic potassium hydroxide* and boil gently under a reflux condenser for thirty minutes; rinse the condenser with *water*, allow to cool, add 2.5 ml of *nitric acid*, 25 ml of *0.1N silver nitrate*, and 5 ml of *dibutyl phthalate*, shake vigorously, and titrate with *0.1N ammonium thiocyanate*, using 5 ml of *ferric ammonium sulphate solution* as indicator. Repeat the operation without the chlorophenothane; the difference between the titrations represents the quantity of *0.1N silver nitrate* required to precipitate the hydrolysable chlorine. Each ml of *0.1N silver nitrate* is equivalent to 0.003545 g of hydrolysable chlorine.

Water-extractives : Not more than 0.25 per cent, determined by the following method: Weigh accurately 20 g, dissolve in 100 ml of *toluene* and transfer to a separator. Add 50 ml of *water* and shake for three minutes. Allow the layers to separate and draw off the *water* into a flask, and stopper the flask immediately. Extract with two further quantities, each of 25 ml of *water*, add the water extracts to the first one and mix. Evaporate 25 ml of the extract and dry at 105° for one hour.

Chloral hydrate : Not more than 0.025 per cent, determined by the following method: Transfer 4.0 ml of the extract prepared as directed under water-extractives to a test-tube and add 2 ml of a 40 per cent w/v solution of *sodium hydroxide* and 1 ml of *pyridine*; any red colour produced is not more intense than that of a blank containing 4 ml of a 0.005 per cent w/v solution of *chloral hydrate* treated in a similar manner.

Sulphated ash : Not more than 0.5 per cent, Appendix 3.2.7.

Assay : Weigh accurately about 1 g, add 40 ml of *benzene*, shake until solution is complete and add sufficient *isopropyl alcohol* to produce 250.0 ml and mix. Pipette 25 ml of the resulting solution into a flask, add 2.5 g of *sodium* in small pieces, connect the flask to a reflux condenser and boil gently for thirty minutes, shaking the flask occasionally. Add *isopropyl alcohol* dropwise through the condenser, until the sodium is consumed. Boil for ten minutes, add 60 ml of *water*, cool, add a few drops of *phenolphthalein solution* and neutralise with *dilute nitric acid*. Add 10 ml of *dilute nitric acid*, cool, and add 25.0 ml of *0.1N silver nitrate* and 5 ml of *dibutylphthalate*. Shake vigorously and titrate with *0.1N ammonium thiocyanate*, using 5 ml of *ferric ammonium sulphate solution* as indicator. Perform a blank determination with the same quantities of the reagents. Each ml of *0.1N silver nitrate* is equivalent to 0.00709 g of $C_{14}H_9Cl_5$.

Storage : Store in well-closed, light-resistant containers.

Chloroquine Phosphate

$C_{18}H_{26}ClN_3,2H_3PO_4$ Mol. Wt. 515.87

Category : Antimalarial, antiprotozoal.

Dose : In the treatment of malaria; suppressive, 500 mg weekly; therapeutic, initial dose, 1 g, subsequent doses, 500 mg daily.

In the treatment of amoebiasis, 500 mg three times a day for two weeks, then 750 mg two times a week for several months.

Description : White or almost white crystalline powder; odourless; taste, bitter. It slowly gets discoloured on exposure to light.

Solubility : Freely soluble in *water*; practically insoluble in *alcohol*, in *chloroform* and in *solvent ether*.

Standards : Chloroquine Phosphate is 7-chloro-4-(4-diethylamino-1-methylbutylamino) quinoline diorthophosphate. It contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of $C_{18}H_{26}ClN_3,2H_3PO_4$, calculated with reference to the dried substance.

Identification : (A) Dissolve 0.1 g in 10 ml of *water*, add 2 ml of *2N sodium hydroxide* and extract with two quantities, each of 20 ml, of *chloroform*, retaining the aqueous layer. Wash the chloroform extracts with *water*, dry with *anhydrous sodium sulphate*, evaporate to dryness, and dissolve the residue in 2 ml of *chloroform*. The *infra-red absorption spectrum* of the chloroform solution exhibits maxima which are only at the same wavelengths as, and have similar relative intensities

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

to, those in the spectrum obtained with the chloroform solution of *chloroquine phosphate R.S.* treated in a similar manner, Appendix 5.15 B.

(B) Dissolve 25 mg in 20 ml of *water*, shake, add 5 ml of *picric acid solution* containing a drop of *N sodium hydroxide*, filter; the precipitate after washing successively with *water*, *alcohol* and *solvent ether* and drying has a melting range between 205° and 210°C, Appendix 5.11.

(C) Neutralise with *dilute nitric acid* the aqueous layer obtained in **Identification** test A. Add an equal volume of *ammonium molybdate solution* and warm; a yellow precipitate is produced.

(D) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.0015 per cent w/v solution in *0.01N hydrochloric acid* exhibits maxima, at 257 nm, 329 nm, and 343 nm; *extinction* at 257 nm, about 0.6, Appendix 5.15A.

pH : Between 3.5 and 4.5 determined in a 10 per cent w/v solution, Appendix 5.10.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel GF 254* as the coating substance and a mixture of 5 volumes of *chloroform*, 4 volumes of *cyclohexane* and 1 volume of *diethylamine* as the mobile phase. Apply separately to the plate 2 µl of each of three solutions of the substance being examined containing (1) 5.0 per cent w/v, (2) 0.050 per cent w/v, and (3) 0.025 per cent w/v. After removal of the plate, allow it to dry in air and examine under an ultra-violet lamp having a maximum output at about 254 nm. Any spot in the chromatogram obtained with solution (1), other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (3), except that one such spot may be not more intense than the spot in the chromatogram obtained with solution (2).

Heavy metals : Not more than 10 parts per million, determined on 2.0 g by Method B, Appendix 3.2.4.

Loss on drying : Not more than 2.0 per cent, determined on 1.0 g by drying in an oven at 105°C, Appendix 5.8.

Assay : Weigh accurately about 0.5 g and dissolve in 40 ml of *glacial acetic acid*. Titrate with *0.1N perchloric acid*, determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02579 g of $C_{18}H_{26}ClN_3, 2H_3PO_4$.

Storage : Store in well-closed, light-resistant containers.

Chloroquine Phosphate Injection

Category : Antimalarial; anti-amoebic.

Dose : By intravenous or intramuscular injection, for an adult, the equivalent of 200 to 300 mg of chloroquine base (antimalarial).

By intramuscular injection, for an adult, the equivalent of 160 to 200 mg of chloroquine base (anti-amoebic).

NOTE – 200 mg of chloroquine base is approximately equivalent to 322 mg of chloroquine Phosphate.

Usual strength : The equivalent of 40 mg of chloroquine base per ml.

Standards : Chloroquine Phosphate Injection is a sterile solution of Chloroquine Phosphate in Water for Injection. It contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of chloroquine, $C_{18}H_{26}ClN_3$.

Identification : (A) To a volume equivalent to 60 mg of chloroquine add 2 ml of *2N sodium hydroxide* and complete **Identification** test (A) described under Chloroquine Phosphate, beginning at the words "and extract with two quantities.....".

(B) Dilute a volume equivalent to 15 mg of chloroquine to 20 ml with *water* and add 8 ml of *picric acid solution*; the precipitate after washing successively with *water*, *alcohol* and *solvent ether* melts at about 207°. Appendix 5.11.

(C) Neutralise with *2N nitric acid* the aqueous layer obtained in **Identification** test A after extraction of the base, add an equal volume of a 10 per cent w/v solution of *ammonium molybdate*, and warm; a yellow precipitate is produced.

pH : Between 3.5 and 4.5, Appendix 5.10.

Other requirements : Complies with the requirements stated under Injections.

Assay : To a volume equivalent to 0.4 g of Chloroquine add 20 ml of *N sodium hydroxide* and extract with four quantities, each of 25 ml, of *chloroform*. Combine the chloroform extracts and evaporate to a volume of about 10 ml. Add 40 ml of *glacial acetic acid* and titrate with *0.1N perchloric acid*, determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.01599 g of chloroquine, $C_{18}H_{26}ClN_3$.

Storage : Store in single-dose containers.

Labelling : The label on the container states the strength as the equivalent amount of chloroquine base in each ml.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Chloroquine Phosphate Tablets

Category : Antimalarial, antiprotozoal.

Dose : Chloroquine Phosphate. In the treatment of malaria: suppressive, 500 mg weekly; therapeutic, initial dose, 1 g, subsequent doses, 500 mg daily.

In the treatment of amoebiasis: 500 mg three times a day for two weeks; then 75 mg two times a week, for several months.

Usual strengths : 100 mg; 250 mg.

Standards : Chloroquine Phosphate Tablets contain not less than 93.0 per cent and not more than 107.0 per cent of the stated amount of Chloroquine Phosphate, $C_{18}H_{26}ClN_3,2H_3PO_4$. The tablets may be coated.

Identification : (A) Dissolve a quantity of the powdered tablets equivalent to 0.1 g of Chloroquine Phosphate in a mixture of 10 ml of *water* and 2 ml of *2N sodium hydroxide* and complete **Identification** test (A) described under Chloroquine Phosphate, beginning at the words "and extract with two quantities.....

(B) Extract a quantity of the powdered tablets equivalent to 25 mg of Chloroquine Phosphate with 20 ml of *water*, filter, and to the filtrate add 8 ml of *picric acid solution*. The precipitate, after washing successively with *water*, *alcohol* and *solvent ether* melts at about 207°, Appendix 5.11.

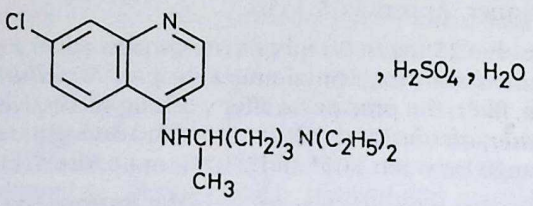
(C) Extract a quantity of the powdered tablets equivalent to 0.5 g of Chloroquine Phosphate with 25 ml of *water* and filter. To the filtrate add 2.5 ml of *5N sodium hydroxide* and extract with three quantities, each of 10 ml, of *solvent ether*. The aqueous layer, after neutralisation with *2N nitric acid* gives the reactions of *phosphates*, Appendix 3.1.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 0.5 g of Chloroquine Phosphate, dissolve in 20 ml of *N sodium hydroxide* and extract with four quantities, each of 25 ml, of *chloroform*. Combine the chloroform extract and evaporate to a volume of about 10 ml. Add 40 ml of *glacial acetic acid* and complete the **Assay** described under Chloroquine Phosphate beginning at the words "Titrate with *0.1N perchloric acid*.....".

Storage : Store in well-closed, light-resistant containers.

Chloroquine Sulphate



$C_{18}H_{26}ClN_3, H_2SO_4, H_2O$ Mol. Wt. 435.96

Category : Antimalarial, anti-amoebic.

Dose : In the treatment of malaria; suppressive, 400 mg weekly; therapeutic, 400 mg to 1.2 g daily.

In the treatment of amoebiasis; 400 to 800 mg daily, in divided doses.

Description : White or almost white crystalline powder; odourless; taste, bitter.

Solubility : Freely soluble in *water*; practically insoluble in *alcohol*; very slightly soluble in *solvent ether* and in *chloroform*.

Standards : Chloroquine Sulphate is the monohydrate of the sulphate of 7-chloro-4-(4-diethylamino-1-methylbutylamino) quinoline. It contains not less than 98.0 per cent of $C_{18}H_{26}ClN_3,H_2SO_4$, calculated with reference to the dried substance.

Identification : (A) Dissolve 0.1 g in 10 ml of *water*, add 2 ml of *2N sodium hydroxide* and extract with two quantities, each of 20 ml, of *chloroform*. Wash the chloroform extracts with *water*, dry with *anhydrous sodium sulphate*, evaporate to dryness, and dissolve the residue in 2 ml of *chloroform*. The *infra-red absorption spectrum* of the chloroform solution exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum obtained with the chloroform solution of *chloroquine sulphate R.S.*, treated in a similar manner, Appendix 5.15 B.

(B) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.001 per cent w/v solution in *0.01N hydrochloric acid* exhibits three maxima, at 257 nm, 329 nm, and 343 nm; *extinction* at 257 nm, about 0.39, at 329 nm, about 0.44, and at 343 nm, about 0.46, Appendix 5.15 A.

(C) Dissolve 25 mg in 20 ml of *water* and add 8 ml of *picric acid solution*; the precipitate after washing successively with *water*, *alcohol* and *solvent ether* melts at about 207°, Appendix 5.11.

(D) A solution (1 in 20) gives the reactions of *sulphates*, Appendix 3.1.

pH : Between 4.0 and 5.0 determined in 10 per cent w/v solution, Appendix 5.10.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Heavy metals : Not more than 20 parts per million, determined by Method A on 1.0 g dissolved in 25 ml of *water*, Appendix 3.2.4.

Chloride : 1.0 g complies with the *limit test for chlorides*, Appendix 3.2.2.

Related substances : Complies with the test described under Chloroquine Phosphate.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Water : Between 3.0 per cent and 5.0 per cent w/w, Appendix 3.3.25.

Assay : Dissolve 0 5 g in 10 ml of *water*, add 20 ml of *N sodium hydroxide* and extract with four quantities, each of 25 ml, of *chloroform*. Combine the chloroform extracts and evaporate to a volume of about 10 ml. Add 40 ml of *glacial acetic acid* and titrate with *0.1N perchloric acid*, using *oracet blue B solution* as indicator. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.0209 g of $C_{18}H_{26}ClN_3, H_2SO_4$.

Storage : Store in well-closed, light-resistant containers.

Chloroquine Sulphate Injection

Category : Antimalarial.

Dose : By intravenous or intramuscular injection the equivalent of 200 to 300 mg of chloroquine base.

40 mg of chloroquine base is approximately equivalent to 55 mg of Chloroquine Sulphate.

Usual strength : The equivalent of 40 mg of chloroquine base per ml.

Standards : Chloroquine Sulphate Injection is a sterile solution of Chloroquine Sulphate in Water for Injection. It contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of chloroquine, $C_{18}H_{26}ClN_3$.

Identification : (A) Complies with **Identification** test (A) described under Chloroquine Phosphate Injection, using a volume equivalent to 70 mg of chloroquine.

(B) Complies with **Identification** test (B) described under Chloroquine Phosphate Injection.

(C) A solution (1 in 20) gives the reactions of *sulphates*, Appendix 3.1.

pH : Between 4.0 and 5.5, Appendix 5.10.

Other requirements : Complies with the requirements stated under Injections.

Assay : Carry out the **Assay** described under Chloroquine Phosphate Injection.

Labelling : The label on the container states the strength as the equivalent amount of chloroquine base in each ml.

Chloroquine Sulphate Tablets

Category : Antimalarial; anti-amoebic.

Dose : Chloroquine Sulphate. In the treatment of malaria; suppressive, 400 mg weekly; therapeutic, 400 mg to 1.2 g daily.

In the treatment of amoebiasis, 400 mg to 800 mg daily, in divided doses.

Usual strength : 200 mg. 200 mg of Chloroquine Sulphate is approximately equivalent to 146 mg of chloroquine base.

Standards : Chloroquine Sulphate Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Chloroquine Sulphate, $C_{18}H_{26}ClN_3, H_2SO_4, H_2O$. The tablets may be coated.

Identification : (A) Dissolve a quantity of the powdered tablets equivalent to 0.1 g of Chloroquine Sulphate in a mixture of 10 ml of *water* and 2 ml of *2N sodium hydroxide* and complete **Identification** test (A) described under Chloroquine Sulphate, beginning at the words "extract with two quantities....".

(B) Extract a quantity of the powdered tablets equivalent to about 0.1 g of Chloroquine Sulphate with 10 ml of *water* and 1 ml of *dilute hydrochloric acid* and filter. Add 1 ml of *barium chloride solution* to the filtrate; a white precipitate is produced.

(C) Comply with **Identification** test (B) described under Chloroquine Phosphate Tablets.

Other requirements : Comply with the requirements stated under Tablets.

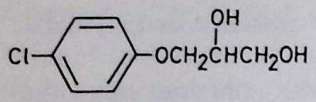
Assay : Carry out the **Assay** described under Chloroquine Phosphate Tablets, using a quantity of the powdered tablets equivalent to 0.5 g of Chloroquine Sulphate. Each ml of *0.1N perchloric acid* is equivalent to 0.0218 g of $C_{18}H_{26}ClN_3, H_2SO_4, H_2O$.

Storage : Store in well-closed, light-resistant containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Chlorphenesin



$C_9H_{11}ClO_3$ Mol. Wt. 202.63

Category : Local antifungal.

Description : White or pale cream-coloured powder; odour, slightly phenolic; taste, bitter and persistent.

Solubility : Slightly soluble in *water*; soluble in *solvent ether*; freely soluble in *alcohol*. Slightly soluble in fixed oils.

Standards : Chlorphenesin is 3-(4-chlorophenoxy)-1, 2-propanediol. It contains not less than 99.0 per cent of $C_9H_{11}ClO_3$, calculated with reference to the dried substance.

Identification : (A) To 1 g add 2 ml of *methyl carbonate* and a few drops of a solution of 0.5 g of *sodium* in 10 ml of *ethyl alcohol*, heat on a water-bath until a gelatinous residue remains, and remove the last traces of solvent by warming under reduced pressure. Dissolve the residue as completely as possible in 10 ml of *ethyl alcohol* with the aid of heat, filter, and allow to cool and crystallise. The crystals, after drying in a current of air melt at about 95°, Appendix 5.11.

(B) Mix 0.5 g with a 1 ml of *sodium hydroxide solution* in a crucible and boil vigorously over a small flame until dry, taking care to avoid charring. Add 4 ml of *water*, boil to dissolve, cool and slowly add 2 ml of *nitric acid*, keeping the mixture cool. The solution gives the reactions of *chlorides*, Appendix 3.1.

(C) The light-absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.01 per cent w/v solution exhibits a maximum only at 280 nm; *extinction* at 280 nm, about 0.65, Appendix 5.15 A.

Melting range : Between 77° and 80°, Appendix 5.11.

Chlorophenol : To 0.1 g dissolved in 5.5 ml of *water*, add 3 ml of a 4 per cent w/v solution of *sodium hexametaphosphate*, 1.5 ml of *lithium and sodium molybdophosphotungstate solution* and 0.4 g of *anhydrous sodium carbonate*, heat on a water-bath for five minutes, and cool. Any blue colour produced is not more intense than that produced when 5.5 ml of a 0.001 per cent w/v solution of *4-chlorophenol* is similarly treated.

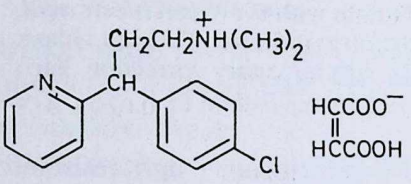
Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying "in vacuo" for 24 hours, Appendix 5.8.

Assay : Weigh accurately about 1.3 g and heat with 15 ml of a 15 per cent v/v solution of *acetic anhydride* in *pyridine* under a reflux condenser on a water-bath for two hours. Cool, add 40 ml of *water* and titrate with *N sodium hydroxide*, using *phenolphthalein solution* as indicator. Repeat the operation without the chlorphenesin; the difference between the titrations represents the amount of *acetic anhydride* required by the chlorphenesin. Each ml of *N sodium hydroxide* is equivalent to 0.1013 g of $C_9H_{11}ClO_3$.

Storage : Store in well-closed containers.

Chlorpheniramine Maleate



$C_{16}H_{19}ClN_2, C_4H_4O_4$ Mol. Wt. 390.87

Category : Antihistaminic.

Dose : 4 to 16 mg daily, in divided doses.

Description : White, crystalline powder; odourless; taste, bitter.

Solubility : Freely soluble in *water*; soluble in *alcohol* and in *chloroform*; slightly soluble in *solvent ether*.

Standards : Chlorpheniramine Maleate is 3-(4-chlorophenyl)-3-(2-pyridyl) propyl-*N*, *N*-dimethylammonium hydrogen maleate. It contains not less than 98.0 per cent of $C_{16}H_{19}ClN_2, C_4H_4O_4$, calculated with reference to the dried substance.

Identification : (A) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.002 per cent w/v solution in *0.1 N sulphuric acid* exhibits a maximum only at 265 nm; *extinction* at 265 nm, about 0.425, Appendix 5.15 A.

(B) Carry out the method described under the test for **Foreign substances**, applying to the plate 2 µl of each of two solutions in *chloroform* containing (1) 0.5 per cent w/v of the substance being examined and (2) 0.5 per cent w/v of *chlorpheniramine maleate R.S.* After removal of the plate, allow it to dry in air, and examine under an ultraviolet lamp having maximum output at about 254 nm. The two principal spots in the chromatogram obtained with solution (1) correspond to those in the chromatogram obtained with solution (2). Spray the plate with *dilute potassium iodobismuthate solution*. The princi-

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

pal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

(C) To 0.5 g in 5 ml of *water*, add 2 ml of *strong ammonia solution*, and extract with three quantities, each of 5 ml, of *chloroform*. Evaporate the aqueous solution to dryness, add 0.2 ml of *dilute sulphuric acid* and 5 ml of *water*, and extract with four quantities, each of 25 ml, of *solvent ether*. Combine the etheral extracts and evaporate the ether in a current of warm air. The residue melts at about 130°, Appendix 5.11.

Melting range : Between 130° and 135°, Appendix 5.11.

pH : Between 4.0 and 5.0, determined in a 1.0 per cent w/v solution, Appendix 5.10.

Foreign substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel GF 254* as the coating substance and heating the coated plate at 105° for thirty minutes. Use as the mobile phase a mixture of 5 volumes of *ethyl acetate*, 3 volumes of *methyl alcohol*, and 2 volumes of *dilute acetic acid*. Apply separately to the plate 2 µl of each of two solutions in *chloroform* containing (1) 5.0 per cent w/v of the substance being examined and (2) 0.01 per cent w/v of the substance being examined. After removal of the plate, allow it to dry in air, and examine under an ultra-violet lamp having a maximum output at about 254 nm. Any spot in the chromatogram obtained with solution (1), other than the two principal spots due to chlorpheniramine and maleic acid, is not more intense than the spot in the chromatogram obtained with solution (2).

Sulphated ash : Not more than 0.15 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.5 g and dissolve in 20 ml of *glacial acetic acid*. Titrate with *0.1N perchloric acid* using *crystal-violet solution* as indicator, until the colour changes from purple to green blue. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.01954 g of $C_{16}H_{19}ClN_2, C_4H_4O_4$.

Storage : Store in tightly-closed, light-resistant containers.

Chlorpheniramine Tablets

Category : Antihistaminic.

Dose : Chlorpheniramine Maleate, 4 to 16 mg daily, in divided doses.

Usual strengths : 4 mg; 8 mg.

Standards : Chlorpheniramine Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Chlorpheniramine Maleate, $C_{16}H_{19}ClN_2, C_4H_4O_4$.

Identification : (A) Shake a quantity of the powdered tablets equivalent to about 30 mg of Chlorpheniramine Maleate for thirty minutes with 15 ml of *solvent ether*, with occasional shaking. Discard the *ether*, shake the residue with three quantities, each of 10 ml, of *solvent ether*, discard the ether, extract the residue with two quantities, each of 15 ml, of *chloroform*, combine the chloroform extracts, add 10 mg of *decolourising charcoal*, shake, filter, and evaporate the filtrate to dryness with the aid of a current of air. The residue after drying at 105°C for one hour, melts at about 130°, Appendix 5.11.

(B) Comply with **Identification** test (B) described under Chlorpheniramine Maleate, using as solution (1) a solution prepared in the following manner: Extract a quantity of the powdered tablets equivalent to 50 mg of Chlorpheniramine Maleate with *chloroform*, filter, and evaporate to dryness; dissolve the residue in 1 ml of *chloroform*.

Foreign substances : Comply with the test described under Chlorpheniramine Maleate, using as solution (1) a solution prepared in the following manner: Extract a quantity of the powdered tablets equivalent to 50 mg of Chlorpheniramine Maleate with *chloroform*, filter, and evaporate to dryness; dissolve the residue in 1 ml of *chloroform*. For solution (2) dilute 1 volume of solution (1) to 500 volumes with *chloroform*.

Uniformity of content : Powder one tablet and carry out the **Assay** beginning at the words "shake with 20 ml of *0.1N sulphuric acid*.....".

Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 90 and 110 per cent of the average except that for one tablet the content may be between 85 and 115 per cent of the average.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 3 mg of Chlorpheniramine Maleate and shake with 20 ml of *0.1N sulphuric acid* for five minutes, add 20 ml *solvent ether*, shake carefully, and filter the acid layer into a second separator. Extract the ether layer with two quantities, each of 10 ml, of *0.1N sulphuric acid*, filtering each acid layer into the second separator, and wash the filter with *0.1N sulphuric acid*. Make the combined acid extracts and washing just alkaline to litmus paper with *N sodium hydroxide*, add 2 ml in excess, and extract with two quantities, each of 50 ml, of *solvent ether*. Wash each ether extract with the same 20 ml of *water* and extract in succession with 20, 20 and 5 ml of *0.5N sulphuric acid*, dilute the combined acid extracts to 50.0 ml with *0.5N sulphuric acid*; dilute 10.0 ml to 25.0 ml with *0.5N*

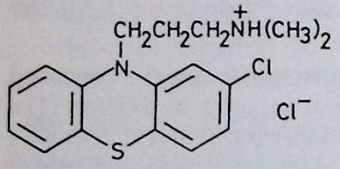
CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

sulphuric acid, and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 265 nm, Appendix 5.15 A. Calculate the content of $C_{16}H_{19}ClN_2,C_4H_4O_4$, taking 212 as the value of E(1 per cent, 1-cm) at the maximum at about 265 nm.

Storage : Store in tightly-closed containers.

Chlorpromazine Hydrochloride



$C_{17}H_{19}ClN_2S, HCl$ Mol. Wt.355.32

Category : Central depressant, tranquilliser; anti-emetic.

Dose : In psychiatric states, 75 to 800 mg daily, in divided doses; by intramuscular injection, 25 to 100 mg.

As an anti-emetic, 25 to 50 mg; by intramuscular injection 25 to 50 mg.

Description : White or creamy-white powder; odourless; taste, very bitter.

Solubility : Soluble in *water*, in *alcohol* and in *chloroform*; practically insoluble in *solvent ether*.

Standards : Chlorpromazine Hydrochloride is 3-(2-chlorophenothiazin-10-yl)propyl-*N*,*N*-dimethyl-ammonium chloride. It contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of $C_{17}H_{19}ClN_2S, HCl$, calculated with reference to the dried substance.

Identification : (A) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a freshly prepared mixture of equal volumes of *solvent ether* and *ethyl acetate* saturated with *strong ammonia solution*. Apply separately to the plate 2 µl of each of the following solutions: (1) a 0.5 per cent w/v solution of the substance being examined in *methyl alcohol*; (2) a 0.5 per cent w/v solution of *chlorpromazine hydrochloride R.S.* in *methyl alcohol*. After removal of the plate, dry it in air and examine under an ultra-violet lamp having a maximum output at about 254 nm. The principal spot in the chromatogram obtained with solution (1) corresponds with that in the chromatogram obtained with solution (2)

(B) Dissolve 5 mg in 5 ml of *sulphuric acid*; a cherry red colour is produced, which darkens slowly on standing; a portion of this solution on warming changes through brown to magenta; the remaining portion on addition of 0.2 ml of *0.1N potassium dichromate* changes to brownish-red.

(C) Dissolve 5 mg in 5 ml of *water* and add one drop of *ferric chloride test-solution*, a stable red colour is produced.

(D) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.0005 per cent w/v solution in *0.1N hydrochloric acid* exhibits a maximum at 254 nm; *extinction* at 254 nm, about 0.46, Appendix 5.15 A.

(E) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

Melting range : Between 194° and 198°, Appendix 5.11.

pH : Between 4.0 and 5.0, determined in a 10 per cent w/v solution, Appendix 5.10.

Related impurities : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel GF 254* as the coating substance and a mixture of 80 volumes of *cyclohexane*, 10 volumes of *acetone* and 10 volumes of *diethylamine*, as the mobile phase. Apply separately to the plate 10 µl of (1) a 2.0 per cent w/v solution of the substance being examined in a mixture of 95 volumes of *methyl alcohol* and 5 volumes of *diethylamine* prepared immediately before use and (2) a 0.01 per cent solution of *chlorpromazine hydrochloride R.S.* dissolved in a mixture of 95 volumes of *methyl alcohol* and 5 volumes of *diethylamine* prepared immediately before use. After removal of the plate, allow it to dry in air and examine under an ultra-violet lamp having a maximum output at about 254 nm. Any spot on the chromatogram obtained with the solution (1) other than the principal spot is not more intense than the spot obtained with solution (2).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.6 g and dissolve in 200 ml of *acetone*. Add 15 ml of *mercuric acetate solution* and titrate with *0.1N perchloric acid*. Using a saturated solution of *methyl orange* in *acetone* as indicator, perform a blank determination and make any necessary correction.

Each ml of *0.1N perchloric acid* is equivalent to 0.03553 g of $C_{17}H_{19}ClN_2S,HCl$.

Storage : Store in well-closed, light-resistant containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Chlorpromazine Injection

Chlorpromazine Hydrochloride Injection

Category : Central depressant, tranquilliser; anti-emetic.

Dose : Chlorpromazine Hydrochloride, in psychiatric state, 25 to 100 mg by intramuscular injection.

As an anti-emetic, 25 to 50 mg by intramuscular injection.

Usual strength : 25 mg per ml.

Standards : Chlorpromazine Injection is a sterile solution of Chlorpromazine Hydrochloride in Water for Injection free from dissolved air and containing suitable buffering and stabilizing agents. It contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of $C_{17}H_{19}ClN_2S$, HCl.

Description : Colourless, or almost colourless solution.

Identification : (A) Complies with **Identification** tests (A) and (B) described under Chlorpromazine Hydrochloride, using a volume equivalent to 5 mg of Chlorpromazine Hydrochloride.

(B) To a volume equivalent to 0.1 g of Chlorpromazine Hydrochloride add sufficient *potassium carbonate* to saturate the solution extract with two quantities, each of 10 ml of *solvent ether*. Evaporate the combined extracts to dryness. Dissolve the residue in 2 ml of *methyl alcohol* and pour into a solution of 0.4 g of *picric acid* in 10 ml of *methyl alcohol* previously warmed to about 50°, cool, scratch the tube to induce crystallisation, allow to stand for three to four hours, and filter. The residue after washing with *methyl alcohol* melts at about 175°, Appendix 5.11.

(C) It gives the reactions of *chlorides*, Appendix 3.1.

pH : Between 5.0 and 6.5, Appendix 5.10.

Related impurities : Complies with the test described under Chlorpromazine Hydrochloride, applying separately to the plate 20 µl of each of the following freshly prepared solutions:For solution (1) dilute a volume of the injection with sufficient mixture of 95 volumes of *methyl alcohol* and 5 volumes of *diethylamine* to produce a solution containing the equivalent of 1.0 per cent w/v of Chlorpromazine Hydrochloride; for solution (2) dilute 1 volume of solution (1) to 200 volumes with the same solvent; for solution (3) dilute 1 volume of solution (1) to 20 volumes with the same solvent. Any spot in the chromatogram obtained with solution (1), other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (2), except that one spot may be more intense than the spot in the chromatogram obtained with soultion (3).

Other requirements : Complies with requirements stated under Injections.

Assay : Dilute an accurately measured volume with sufficient *0.1N hydrochloric acid* to produce a solution containing about 0.0005 per cent w/v of Chlorpromazine Hydrochloride and measure the *extinction* of 1-cm layer of the resulting solution at the maximum at about 254 nm, Appendix 5.15 A. Calculate the content of $C_{17}H_{19}ClN_2S$,HCl taking 915 as the value of E(1 per cent, 1-cm) at the maximum at about 254 nm.

Storage : Store in single-dose or multiple-dose, light-resistant containers.

Chlorpromazine Tablets

Chlorpromazine Hydrochloride Tablets

Category : Central depressant, tranquilliser; anti-emetic.

Dose : Chlorpromazine Hydrochloride. As an anti-emetic, 25 to 50 mg daily, in divided doses. In psychiatric states, 75 to 800 mg daily, in divided doses.

Usual strengths : 10 mg; 25 mg; 50 mg; 100 mg; 200 mg.

Standards : Chlorpromazine Tablets contain not less than 92.5 per cent and not more than 107.0 per cent of the stated amount of Chlorpromazine Hydrochloride, $C_{17}H_{19}ClN_2S$, HCl. The tablets are coated.

Identification : (A) Digest a quantity of the powdered tablets equivalent to about 25 mg of Chlorpromazine Hydrochloride with 25 ml of *water* and filter; the solution so obtained complies with **Identification** tests (B) to (E) described under Chlorpromazine Hydrochloride.

(B) Comply with **Identification** test (B) described under Chlorpromazine Hydrochloride, using as solution (1) a solution prepared in the following manner: Shake a quantity of the powdered tablets with sufficient *methyl alcohol* to produce a solution containing 0.5 mg of Chlorpromazine Hydrochloride per ml, centrifuge, and use the supernatant liquid.

Uniformity of content : For tablets containing 10 mg of Chlorpromazine Hydrochloride.

NOTE – Protect the solution from light throughout the test.

Powder one tablet, shake with 1 ml of *dilute hydrochloric acid* and 40 ml of *water*. Shake for fifteen minutes, add sufficient *water* to produce a 100.0 ml and mix; centrifuge about 15 ml of the mixture. To 10.0 ml of clear supernatant liquid add 2 ml of *N hydrochloric acid*,

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

and sufficient *water* to produce a solution containing about 0.0005 per cent w/v of Chlorpromazine Hydrochloride. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 254 nm, Appendix 5.15 A. Calculate the content of $C_{17}H_{19}ClN_2S$, HCl taking 915 as the value of E(1 per cent, 1-cm) at the maximum at about 254 nm.

Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 90 per cent and 110 per cent of the average except that for one tablet the content may be between 85 per cent and 115 per cent of average.

Related impurities : Comply with the test described under Chlorpromazine Hydrochloride, using the following freshly prepared solutions: For solution (1) extract a quantity of the powdered tablets equivalent to 0.1 g of Chlorpromazine Hydrochloride with 10 ml of a mixture of 95 volumes of *methyl alcohol* and 5 volumes of *diethylamine* and filter; for solution (2) dilute 1 volume of solution (1) to 200 volumes with the same solvent mixture.

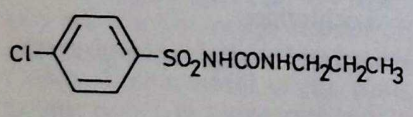
Other requirements : Comply with the requirements stated under Tablets.

Assay : Protect the solution from light throughout the assay.

Weigh 20 tablets or more, if necessary and reduce to a *fine powder*. Weigh accurately a quantity of powder equivalent to about 0.1 g of Chlorpromazine Hydrochloride, add 5 ml of *dilute hydrochloric acid* and 200 ml of *water*. Shake for fifteen minutes, add sufficient *water* to produce 500.0 ml, and centrifuge about 50 ml of the mixture. To 5.0 ml of the clear, supernatant liquid add 10 ml of *N hydrochloric acid* and sufficient *water* to produce 200.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 254 nm, Appendix 5.15 A. Calculate the content of $C_{17}H_{19}ClN_2S$, HCl, taking 915 as the value of E(1 per cent, 1-cm) of the maximum at about 254 nm.

Storage : Store in well-closed, light-resistant containers.

Chlorpropamide



$C_{10}H_{13}ClN_2O_3S$ Mol. Wt. 276.74

Category : Antidiabetic.

Dose : 100 to 500 mg daily.

Description : White, crystalline powder; odourless or almost odourless; almost tasteless.

Solubility : Practically insoluble in *water*; soluble in *alcohol*; sparingly soluble in *chloroform*; slightly soluble in *solvent ether*; also soluble in solutions of alkali hydroxides.

Standards : Chlorpropamide is 1-(4-chlorobenzenesulphonyl)-3-propylurea. It contains not less than 97.0 per cent and not more than the equivalent of 101.0 per cent of $C_{10}H_{13}ClN_2O_3S$, calculated with reference to the dried substance.

Identification : (A) Boil 0.1 g with 8 ml of a 50 per cent w/w solution of *sulphuric acid* under a reflux condenser for thirty minutes, cool, and filter, reserving the filtrate. The precipitate, after recrystallisation from *water* melts at about 143°, Appendix 5.11.

(B) Make the filtrate reserved in **Identification** test A alkaline with *sodium hydroxide solution* and heat; an ammoniacal odour is produced.

(C) Heat 1.0 g with *anhydrous sodium carbonate* at a dull red heat for ten minutes. Cool, extract the residue with *water*, and filter. Acidify the filtrate with *dilute nitric acid* and add *silver nitrate solution*; a white precipitate is produced.

(D) Dissolve about 0.16 g in 50 ml of *methyl alcohol*, dilute 5 ml to 100 ml with *0.01N hydrochloric acid* and dilute 5 ml of this solution to 100 ml with *0.01N hydrochloric acid*. The light absorption, in the range 230 to 350 nm, of a 1-cm layer of the resulting solution, exhibits a maximum only at about 232 nm; *extinction* at 232 nm, about 0.48, Appendix 5.15 A.

Melting range : Between 125° and 130°, Appendix 5.11.

Heavy metals : Not more than 30 parts per million, determined on 0.66 g by Method B, Appendix 3.2.4.

Foreign substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 15 volumes of *isopropyl alcohol*, 3 volumes of *cyclohexane*, 1 volume of *strong ammonia solution* and 1 volume of *water* as the mobile phase. Apply separately to the plate 5 µl of each of three solutions in *acetone* containing (1) 6.0 per cent w/v of the substance being examined; (2) 0.02 per cent w/v of *p-chlorobenzenesulphomide R.S.*; (3) 0.02 per cent w/v of *N,N' dipropylurea R.S.*; (4) 0.02 per cent w/v of *p-chlorobenzenesulphonylurea R.S.* After removal of the plate, dry it in a current of warm air, heat at 110° for ten minutes, and spray the hot plate with *sodium hypochlorite solution* diluted with *water* to contain 0.5 per cent w/v of available chlorine. Dry in a current of cold air until a sprayed area of the plate below the line of application gives at most a very faint blue colour with a drop of a 0.5 per cent w/v solution of *potassium iodide* in *starch solution*; avoid prolonged exposure to cold air. Spray the plate with a 5 per cent w/v solution of *potassium iodide*

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

in *starch solution*. The spots in the chromatograms obtained with solutions (2), (3) and (4) are more intense than any corresponding spots in the chromatogram obtained with solution (1).

Loss on drying : Not more than 1.5 per cent, determined on 1.0 g by drying "in vacuo at 60°" for two hours, Appendix 5.8.

Sulphated ash : Not more than 0.2 per cent, Appendix 3.2.7.

Assay : Weigh accurately about 0.5 g and dissolve in 50 ml of *alcohol*, previously neutralised to *phenolphthalein solution*. Add 25 ml of *water*, and titrate with *0.1N sodium hydroxide* using *phenolphthalein solution* as indicator. Each ml of *0.1N sodium hydroxide* is equivalent to 0.02767 g of $C_{10}H_{13}ClN_2O_3S$.

Storage : Store in well-closed containers.

Chlorpropamide Tablets

Category : Antidiabetic.

Dose : Chlorpropamide, 100 to 500 mg daily.

Usual strengths : 100 mg; 250 mg.

Standards : Chlorpropamide Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Chlorpropamide, $C_{10}H_{13}ClN_2O_3S$.

Identification : Extract a quantity of the powdered tablets equivalent to about 1.0 g of Chlorpropamide with five quantities, each of 4 ml, of *acetone*, filter, and evaporate carefully to dryness on a water-bath. The residue complies with **Identification** tests (A) to (C) described under Chlorpropamide.

Disintegration : Not more than thirty minutes, Appendix 5.6.1.

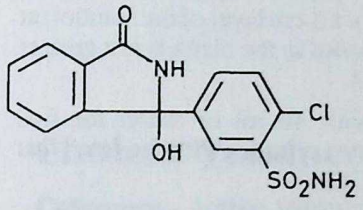
Dissolution : Comply with the *dissolution test for tablets and capsules*, Appendix 5.7, using as the medium 1000 ml of a 0.68 per cent w/v solution of *potassium dihydrogen phosphate* adjusted to pH 7.4 by the addition of *N sodium hydroxide* and placing one tablet in the basket for each test. Withdraw a sample of 10 ml of the medium and filter. Measure the *extinction* of the filtrate, suitably diluted if necessary with *0.1N hydrochloric acid* at the maximum at about 232 nm, Appendix 5.15 A. Calculate the total content of $C_{10}H_{13}ClN_2O_3S$, in the medium, taking 598 as the value of E(1 per cent, 1-cm) at the maximum at about 232 nm.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.25 g of Chlorpropamide and shake with 40 ml of *methyl alcohol* for twenty minutes, add sufficient *methyl alcohol* to produce 50.0 ml, mix, filter and dilute 5.0 ml of the filtrate to 100.0 ml with *0.1N hydrochloric acid*. Mix, dilute 10.0 ml of this solution to 250.0 ml with *0.1N hydrochloric acid* and measure the *extinction* of the resulting solution at the maximum at about 232 nm, Appendix 5.15 A. Calculate the content of $C_{10}H_{13}ClN_2O_3S$, taking 598 as the value of E(1 per cent, 1-cm) at the maximum at about 232 nm.

Storage : Store in well-closed containers.

Chlorthalidone



$C_{14}H_{11}ClN_2O_4S$ Mol. Wt. 338.76

Category : Diuretic.

Dose : 100 to 200 mg daily.

Description : White to yellowish-white, crystalline powder; almost odourless; tasteless.

Solubility : Practically insoluble in *water*, in *solvent ether* and in *chloroform*; slightly soluble in *alcohol*; soluble in *methyl alcohol* and in solutions of alkali hydroxides.

Standards : Chlorthalidone is 2-chloro-5-(3-hydroxy-1-oxoisoindolin-3-yl) benzenesulphonamide. It contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of $C_{14}H_{11}ClN_2O_4S$, calculated with reference to the dried substance.

Identification : (A) Dissolve about 50 mg in 3 ml of *sulphuric acid*; an intense yellow colour is produced.

(B) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.01 per cent w/v solution in *alcohol* exhibits two maxima at 275 nm and at 284 nm; *extinction* at 275 nm, about 0.6, and at 284 nm, about 0.45, Appendix 5.15 A.

(C) Burn 20 mg by the *oxygen-flask method*, Appendix 3.3.6, using 5 ml of *dilute sodium hydroxide solution* as the absorption liquid. When the process is complete, dilute the liquid to 25 ml with *water*. To 5 ml of the solution so obtained, add 0.1 ml of *strong hydrogen peroxide solution* and 1 ml of *N hydrochloric acid*, mix,

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

and add 0.05 ml of *barium hydroxide solution*; a turbidity is produced. To a further 5 ml of the solution obtained as described above add sufficient *dilute sulphuric acid* to make it acid and boil gently for two minutes; solution gives the reactions of *chlorides*, Appendix 3.1.

(D) It melts at about 220° with decomposition, Appendix 5.11.

Acidity : Dissolve 1.0 g in 5 ml of *dioxan* with the aid of gentle heat, cool, add 25 ml of *water*, and titrate with *0.1N sodium hydroxide*, using *methyl red solution* as indicator. Repeat the operation without the substance being examined. The difference between the titrations is not more than 0.9 ml.

Clarity and colour of solution : Dissolve 1.0 g in sufficient *methyl alcohol* to produce 25 ml. The solution is clear and the *extinction* of a 1-cm layer of the solution at 410 nm against *methyl alcohol* as the blank is not greater than 0.01, Appendix 5.15 A.

Chloride : Shake 1.0 g with 40 ml of *water* for five minutes and filter; the filtrate complies with the *limit test for chlorides*, Appendix 3.2.2.

Foreign substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel GF 254* as the coating substance and a mixture of 15 volumes of *n-butyl alcohol* and 3 volumes of *N ammonia* as the mobile phase. Apply separately to the plate 10 µl of each of two solutions in *methyl alcohol* containing (1) 1.0 per cent w/v of the substance being examined and (2) 0.01 per cent w/v of *2-(4-chloro-3-sulphamoylbenzoyl) benzoic acid R.S.* After removal of the plate, allow it to dry in air and examine under an ultra-violet lamp having a maximum output at about 254 nm. Any spot in the chromatogram obtained with solution (1) other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (2).

Heavy metals : Not more than 10 parts per million, determined on 2.0 g by Method B, Appendix 3.2.4.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.3 g and dissolve in 50 ml of *dehydrated pyridine*. Titrate with *0.1N tetrabutylammonium hydroxide*, determining the end-point potentiometrically and protecting the solution and titrant from atmospheric carbon dioxide throughout the determination. Perform a blank determination and make any necessary correction. Each ml of *0.1N tetrabutylammonium hydroxide* is equivalent to 0.03388 g of $C_{14}H_{11}ClN_2O_4S$.

Storage : Store in well-closed containers.

Chlorthalidone Tablets

Category : Diuretic.

Dose : Chlorthalidone, 100 mg to 200 mg daily.

Usual strength : 50 mg.

Standards : Chlorthalidone Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Chlorthalidone, $C_{14}H_{11}ClN_2O_4S$.

Identification : (A) Boil a quantity of the powdered tablets equivalent to 0.2 g of Chlorthalidone with 5 ml of *acetone*, filter, add 40 ml of *water* to the filtrate, and allow to stand. The crystals, after washing with *water* comply with **Identification** test (A) described under Chlorthalidone.

(B) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of the solution obtained in the **Assay** exhibits maxima at 275 nm and at 284 nm, Appendix 5.15 A.

Foreign substances : Comply with the test described under Chlorthalidone, using as solution (1) a solution prepared in the following manner: Shake a quantity of the powdered tablets equivalent to 50 mg of Chlorthalidone with 5 ml of *methyl alcohol*, centrifuge, and use the supernatant liquid.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.1 g of Chlorthalidone, boil with 30 ml of *methyl alcohol* under a reflux condenser for five minutes, shake vigorously for fifteen minutes, cool and filter; wash the residue and filter with *methyl alcohol*, and dilute the combined filtrate and washings to 100.0 ml with *methyl alcohol*. To 5.0 ml add 2 ml of *N hydrochloric acid* and sufficient *methyl alcohol* to produce 50.0 ml and measure the *extinction* of the resulting solution at the maximum at about 275 nm, Appendix 5.15 A. Calculate the content of $C_{14}H_{11}ClN_2O_4S$, taking 57.4 as the value of E(1 per cent, 1-cm) at the maximum at about 275 nm.

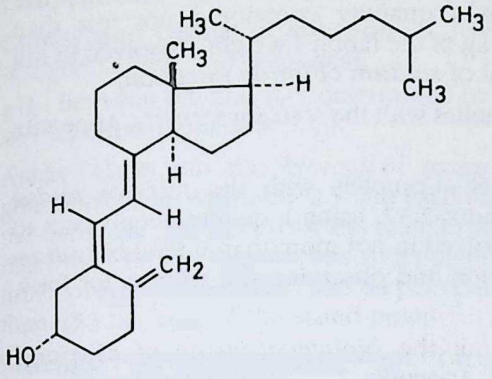
Storage : Store in well-closed containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Cholecalciferol

Vitamin D_3



$C_{27}H_{44}O$ Mol. Wt. 384.64

Category : Antirachitic Vitamin.

Dose : Prophylactic, 400 to 1000 Units daily. Therapeutic, 5000 to 50,000 Units daily, in the treatment of hypoparathyroidism, 50,000 to 200,000 Units daily.

Description : White or almost white crystals; odourless or almost odourless. It is affected by air and by light.

Solubility : Practically insoluble in *water*; freely soluble in *alcohol*, in *chloroform*, in *solvent ether* and in *acetone*, soluble in fixed oils.

Standards : Cholecalciferol is 9, 10-secocholesta - 5, 7, 10(19)-trien-3β-ol. Cholecalciferol contains in 1 mg 40,000 Units of antirachitic activity (Vitamin D).

Identification : (A) Dissolve 1 mg in 1 ml *ethylene chloride* and add 4 ml of *antimony trichloride solution*; a yellowish-orange colour develops.

(B) To a solution of about 0.5 mg in 5 ml of *chloroform* add 0.3 ml of *acetic anhydride* and 0.1 ml *sulphuric acid* and shake vigorously; a bright red colour is produced, and it rapidly changes through violet and blue to green.

(C) Carry out in subdued light the method for *thin-layer chromatography*, Appendix 5.4.3, using a suitable silica gel as the coating substance and a mixture of equal volumes of *cyclohexane* and *solvent ether* as the mobile phase. Apply to the plate 10 µl of each of the following two solutions freshly prepared in *chloroform* containing 1 per cent w/v of *hydroquinone*: (1) 50 mg of the substance being tested and (2) 50 mg of *cholecalciferol R.S.* Remove the plate, allow the solvent to evaporate and spray with a 1 in 50 solution of *antimony trichloride* in *acetyl chloride*. A distinct yellowish-orange spot appears in the chromatogram obtained with solution (1) that corresponds with the spot in the chromatogram obtained with solution (2).

Melting range : Between 82°and 87°, omitting powdering and drying of the substance, Appendix 5.11.

Specific optical rotation : Between +105° and +112°, determined in a solution freshly prepared by dissolving 0.125 g, in *aldehyde-free alcohol* and diluting to 25.0 ml with *aldehyde-free alcohol*, Appendix 5.12.

Light absorption : Dissolve, without the aid of heat, 10 mg in 100.0 ml of *aldehyde-free alcohol*, and dilute 5.0 ml to 50.0 ml with *aldehyde-free alcohol. Extinction* of a 1-cm layer of the resulting solution at the maximum at about 265 nm, determined without delay, 0.465 to 0.495, Appendix 5.15 A.

Storage : Store in hermetically sealed light-resistant containers from which air has been removed or replaced by an inert gas; keep in a cool place.

Cholera Vaccine

Category : Active immunising agent.

Dose : Prophylactic. By subcutaneous injection, initial, 0.5 ml; second dose, 1 ml after an interval of four to six weeks.

Standards : Cholera Vaccine is a sterile suspension of killed cholera Vibrios *(Vibrio cholerae)* of a strain or strains selected for high antigenic efficiency and purity.

The vaccine consists of equal parts of vaccines prepared from smooth strains of two classical types of *Vibrio cholerae*, Inaba and Ogawa. Either a single strain or several strains of each type may be used. All strains must contain, in addition to their type O antigens, the heat-stable O antigen common to Inaba and Ogawa. If more than one strain each of Inaba and Ogawa are used, these may be selected so as to contain other O antigens in addition. Each strain is grown separately. The bacteria may be killed either by heat or by treatment with a bactericide such as phenol or formaldehyde. The vaccine may contain a preservative. It contains not less than 12,000 million bacteria per human dose which does not exceed 1 ml. The vaccine may contain a suitable preservative.

Description : Colourless, whitish or slightly coloured opalescent liquid, free from clumps.

Identification : The organisms are identified by specific agglutination.

pH : Between 6.8 and 7.4, Appendix 5.10.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Phenol (if present) : Not more than 0.5 per cent w/v, Appendix 3.3.9.

Sterility : Complies with the *tests for sterility*, Appendix 4.6.

Undue toxicity : Complies with the *tests for undue toxicity for vaccines and sera*, Appendix 2.37, when injected subcutaneously into the test animals.

Storage : Store at a temperature between 2° and 8°

Labelling : The label on the container states (1) the number of bacteria in each human dose; (2) the storage conditions; (3) "Not to be frozen"; (4) the date after which it is not intended to be used; (5) "shake well before use"; (6) the name and proportion of any added preservative.

Chorionic Gonadotrophin

Human Chorionic Gonadotrophin

Category : Gonadotrophic hormone.

Dose : By intramuscular injection, 500 to 5000 Units, twice weekly.

Description : White or almost white powder.

Solubility : Soluble in *water*; insoluble in *alcohol* in *acetone* and in *solvent ether*.

Standards : Chorionic Gonadotrophin is a dry, sterile preparation of a glycoprotein fraction obtained from the urine of pregnant women. It contains the urinary derivative of the gonadotrophic hormone secreted by the foetal placenta that stimulates the continual functioning of the corpus luteum. It contains not less than 1500 Units per mg.

Identification : Causes enlargement of the prostate gland of immature male rats when administered as directed in the **Assay**.

Clarity and colour of solution : A 1.0 per cent w/v solution is clear and colourless.

Absence of oestrogens : Inject subcutaneously into each of three rats or mice ovariectomised at least two weeks before the test, a single dose of not less than 100 Units dissolved in 0.5 ml of *sodium chloride injection*. Vaginal smears taken on the third, fourth, and fifth days after injection show no signs of a positive response. Using a small platinum wire loop, previously flamed and dipped in *water*, take the smear gently and not too deeply from the posterior vaginal wall and smear across a clean slide in a drop of *water*. Fix the preparation in *methyl alcohol* for three minutes, dry, stain with Giemsa stain, wash in *water*, and allow to dry. The response is positive when most of the cells present in any of the smears are cornified; nucleated cells may be present but leucocytes are absent or scanty.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36 using a quantity containing not less than 1500 Units per kg of the rabbit's weight, dissolved in not more than 1 ml of *sodium chloride injection*.

Sterility : Complies with the *tests for sterility*, Appendix 4.6.

Undue toxicity : Complies with the *test for undue toxicity*, Appendix 2.37, using a quantity equivalent to 1000 Units dissolved in not more than 0.5 ml of *sodium chloride injection* and observing the animals for forty-eight hours.

Assay : Carry out the *biological assay of chorionic gonadotrophin*, Appendix 2.7. The estimated potency is not less than 80 per cent and not more than 125 per cent of the stated potency. The fiducial limits of error are not less than 64 per cent and not more than 156 per cent of the stated potency.

Storage : Store in well-closed, light-resistant containers, sealed so as to exclude micro-organisms and in a cold place.

Labelling : The label on the container states (1) the number of Units contained in it; (2) the number of Units per mg; (3) the date after which the preparation is not intended to be used; (4) the storage conditions.

Chorionic Gonadotrophin Injection

Category : Gonadotrophic hormone.

Dose : By intramuscular injection, 500 to 5000 Units, twice weekly, in accordance with the needs and response of the patient.

Standards : Chorionic Gonadotrophin Injection is a sterile solution of Chorionic Gonadotrophin in Water for Injection. It is prepared by dissolving the contents of a sealed container in the requisite amount of Water for Injection immediately before use. It may contain added buffers, diluents or other inert substances such as Lactose or Sodium Chloride. It may also contain an antimicrobial agent.

Uniformity of weight : Complies with the requirement for **Uniformity of weight**, under Injection.

The contents of the sealed container comply with the requirements for **Identification, Pyrogens, Sterility**

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

and **Undue toxicity** stated under Chorionic Gonadotrophin and with the following requirements:

Description : White or almost white powder.

Clarity and colour of solution : A 1.0 per cent w/v solution is clear and colourless.

pH : Between 6.0 and 8.0, determined in a 1.0 per cent w/v solution, Appendix 5.10.

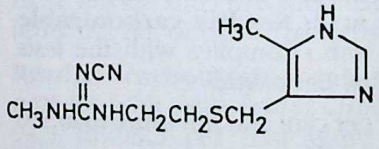
Assay : Carry out the *biological assay of chorionic gonadotrophin*, Appendix 2.7. For each container tested, the estimated potency is not less than 80 per cent and not more than 125 per cent of the stated potency. The fiducial limits of error are not less than 64 per cent and not more than 156 per cent of the stated potency.

Storage : Store in light-resistant containers, sealed so as to exclude micro-organisms and in a cool place.

NOTE – The Injection should be used immediately after preparation.

Labelling : The label on the sealed container states (1) the number of Units contained in it; (2) the name of any added substance; (3) the date after which the preparation is not intended to be used; (4) the storage conditions.

Cimetidine



$C_{10}H_{16}N_6S$ Mol.Wt. 252.33

Category : H_2-receptor antagonist.

Dose : Oral, 200 mg increasing to 400 mg when necessary, 3 times a day, and 400 mg at night; by intravenous injection, 200 mg every 4 to 6 hours. The oral and parenteral dose should not exceed 2 g daily.

Description : White to off-white crystalline powder; odourless or almost odourless.

Solubility : Slightly soluble in *water* and in *acetone*; soluble in warm *alcohol*, in *methyl alcohol* and in dilute mineral acids; practically insoluble in *benzene*, in *chloroform* and in *solvent ether*.

Standards : Cimetidine is 2-cyano-3-methyl-1-[2-(5-methyl-4-imidazolylmethylthio)-ethyl] guanidine. It contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of $C_{10}H_{16}N_6S$, calculated with reference to the dried and solvent-free substance.

Identification : (A) The *infra-red absorption spectrum* of a liquid paraffin dispersion exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *cimetidine R.S.*, Appendix 5.15 B.

(B) It melts at about 142°C, Appendix 5.11.

(C) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 10 volumes of *alcohol*, 1 volume of *methyl alcohol* and 1 volume of *ammonia solution* as the mobile phase. Apply separately to the plate, 5 µl of each of the following two solutions in *methyl alcohol*: (1) 0.2 per cent w/v of the substance being examined and (2) 0.2 per cent w/v of *cimetidine R.S.* After removal of the plate, allow it to dry in air and expose to iodine vapour for 30 to 60 minutes. The principal spot obtained in the chromatogram from solution (1) corresponds in size and intensity with the spot obtained in the chromatogram from solution (2).

(D) The light absorption, in the range 210 to 320 nm, of a 0.0008 per cent w/v solution in *0.1N sulphuric acid* exhibits a maximum at 218 nm, and a minimum at 260 nm, Appendix 5.15 A.

Heavy metals : Not more than 20 parts per million, determined by Method B on 1.0 g, Appendix 3.2.4.

Polymorph B : Not more than 1.5 per cent w/w, determined by the following method: Using a few mg of the finely powdered material, prepare a disc with *potassium bromide IR* and record the *infra-red absorption spectrum*, Appendix 5.15 B, over the range 1100 cm^{-1} to 1200 cm^{-1}. Repeat the operation using a disc prepared with *cimetidine (polymorph B) R.S.* Measure the heights of the peaks occurring at the maximum in the range 1100 cm^{-1} to 1200 cm^{-1} and calculate the content of polymorph B in the substance being examined.

Solvent : Not more than 2.0 per cent w/w, determined by the following method: Carry out the method for *gas-liquid chromatography*, Appendix 5.4.1, using the following solutions in *water* containing: (1) 0.02 per cent v/v of *ethyl alcohol*, 0.02 per cent v/v of *isopropyl alcohol* and 0.02 per cent v/v of *n-butyl alcohol* (internal standard), (2) 1.0 per cent w/v of the dried substance being examined in a mixture of 10 ml of *0.01N sulphuric acid* and 90 ml of *water*, and (3) 1.0 per cent w/v of the dried substance being examined in a mixture of 10 ml of *0.01N sulphuric acid* and 90 ml of *water* and the same concentration of the internal standard as in solution (1). The chromatographic procedure may be carried out using: (a) a column 1.5 m long and 4 mm in internal diameter packed with porous polymer beads (80 to 100 mesh) (Porapak Q is suitable) maintained at 135°; (b) nitrogen as the carrier gas, and (c) a flame ionisation

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

detector. Calculate the percentage w/w of *ethyl alcohol* or *isopropyl alcohol*, assuming the weight per ml at 25°, to be, 0.787 g or 0.782 g respectively.

Sulphated ash : Not more than 0.2 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.25 g and dissolve in 75 ml of *glacial acetic acid*. Titrate with *0.1N perchloric acid* determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02523 g of $C_{10}H_{16}N_6S$.

Storage : Store in well-closed containers.

Cimetidine Tablets

Category : H_2-receptor antagonist .

Dose : Cimetidine 200 mg increasing to 400 mg, three times a day and 400 mg at night.

Usual strength : 200 mg.

Standards : Cimetidine Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Cimetidine, $C_{10}H_{16}N_6S$.

Identification : (A) Shake a quantity of the powdered tablets equivalent to 20 mg of Cimetidine with 20 ml of *alcohol*, filter, evaporate the filtrate to dryness and dry the residue at 100° The *infra-red absorption spectrum* of the dried residue exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *cimetidine R.S.*, Appendix 5.15 B.

(B) Comply with **Identification** test (C) described under Cimetidine, using for solution (A) a solution obtained by shaking a quantity of the powdered tablets equivalent to 2 mg of Cimetidine in 100 ml of a mixture of 10 volumes of *alcohol*, 1 volume of *methyl alcohol* and 1 volume of strong *ammonia solution* and filtering.

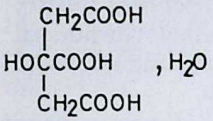
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powdered tablets equivalent to 0.3 g of Cimetidine and stir with 20 ml of warm *methyl alcohol*. Filter and repeat the extraction with three quantities, each of 20 ml of warm *methyl alcohol*. Wash the filter with 20 ml of *methyl alcohol*. Evaporate the combined filtrate and washings to dryness, dissolve the residue in 75 ml of *glacial acetic acid*. Titrate with *0.1N perchloric acid*, determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02523 g of $C_{10}H_{16}N_6S$.

Storage : Store in well-closed containers.

Citric Acid

Citric Acid Monohydrate



$C_6H_8O_7,H_2O$ Mol. Wt. 210.14

Category : Pharmaceutical aid, anticoagulant for storage of whole blood (along with sodium citrate).

Description : Colourless crystals or white crystalline powder; slightly efflorescent in warm dry air.

Solubility : Very soluble in *water*; freely soluble in *alcohol*; sparingly soluble in *solvent ether*.

Standards : Citric Acid is the monohydrate of 2-hydroxy-1,2,3-propane-tricarboxylic acid. It contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of $C_6H_8O_7$, calculated with reference to the anhydrous substance.

Identification; Arsenic; Heavy metals; Copper and iron; Sulphate; Oxalic acid; Readily carbonisable substances; Sulphated ash : Complies with the tests described under Anhydrous Citric Acid

Water : Not less than 7.5 per cent and not more than 9.0 per cent w/w, Appendix 3.3.25.

Assay : Carry out the **Assay** described under Anhydrous Citric Acid. Each ml of *N sodium hydroxide* is equivalent to 0.06403 g of $C_6H_8O_7$.

Storage : Store in tightly-closed containers.

Anhydrous Citric Acid

$C_6H_8O_7$ Mol. Wt. 192.12

Category : Pharmaceutical aid; anticoagulant for storage of whole blood (along with sodium citrate).

Description : Colourless crystals or white powder, odourless; taste, strongly acid. Slightly hygroscopic in moist air.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Solubility : Very soluble in *water*, freely soluble in *alcohol* and slightly soluble in *solvent ether.*

Standards : Anhydrous Citric Acid contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of $C_6H_8O_7$, calculated with reference to the anhydrous substance.

Identification : A solution is strongly acid and when neutralised gives the reactions of *citrates*, Appendix 3.1.

Arsenic : Not more than 1 part per million, Appendix 3.2.1.

Heavy metals : Not more than 10 parts per million, determined on 2.0 g by Method A, Appendix 3.2.4.

Copper and Iron : Dissolve 2.0 g in 40 ml of *water* and 10 ml of *dilute ammonia solution* and 5 drops of *sodium sulphide solution*; the colour produced is only slightly deeper than that produced in a similar mixture containing in addition 1 ml of *potassium cyanide solution Sp.*

Sulphate : 2.0 g complies with the *limit test for sulphates*, Appendix 3.2.8.

Oxalic acid : Dissolve 0.4 g in 4 ml of *water*, add 2 ml of *hydrochloric acid* and 1 g of *granulated zinc* and heat in a water-bath for one minute. Allow to stand for two minutes, decant the liquid into a test-tube containing 0.25 ml of a 1 per cent w/v solution of *phenylhydrazine hydrochloride* and heat to boiling. Cool rapidly, transfer to a graduated measuring cylinder, add an equal volume of *hydrochloric acid* and 0.25 ml of a 5 per cent w/v solution of *potassium ferricyanide*, shake, and allow to stand for thirty minutes. Any red colour produced is not more intense than that produced by carrying out the test using 0.2 mg of *oxalic acid* dissolved in 4 ml of *water.*

Readily carbonisable substances : Heat 0.50 g of powder, with 5 ml of *sulphuric acid* (containing between 94.5 to 95.5 per cent w/w of H_2SO_4) in a boiling water-bath in the dark. Shake after one minute, continue heating for a total of one hour and cool rapidly and immediately. Any colour produced is not deeper than that of the mixture of 0.6 ml of *cobalt chloride C.S.* and 5.4 ml of *ferric chloride C.S.*

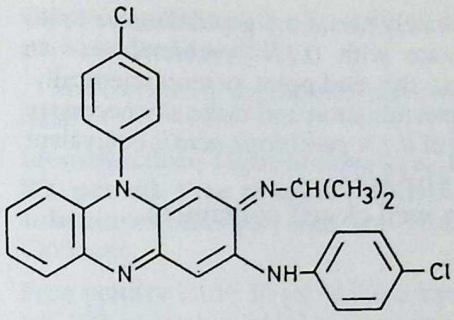
Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Water : Not more than 1.0 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately about 3 g and dissolve in 100 ml of *water.* Titrate with *N sodium hydroxide* using *phenolphthalein solution* as indicator. Each ml of *N sodium hydroxide* is equivalent to 0.06404 g of $C_6H_8O_7$.

Storage : Store in tightly-closed containers.

Clofazimine



$C_{27}H_{22}Cl_2N_4$ Mol. Wt. 473.41

Category : Antibacterial (leprostatic).

Dose : For leprosy, previously untreated patients, 100 mg three times weekly; sulphone-resistant patients 100 mg six times weekly. For the suppression of lepra reactions, 200 mg daily.

Description : Dark red crystals or brownish-red, crystalline powder; nearly odourless.

Solubility : Insoluble in *water*; slightly soluble in *alcohol*; soluble in *dioxan* and in *dimethylformamide.*

Standards : Clofazimine is 3-(4-chloroanilino)-10-(4-chlorophenyl)-2,10-dihydro-2-(isopropylimino) phenazine. It contains not less than 98.5 per cent and not more than the equivalent of 101.5 per cent of $C_{27}H_{22}Cl_2N_4$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *clofazimine R.S.*, Appendix 5.15 B.

(B) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.0002 per cent w/v solution in *methyl alcohol* exhibits a maximum only at 283 nm; *extinction* at 283 nm, about 0.3, Appendix 5.15 A.

(C) Dissolve 10 mg in about 30 ml of *alcohol*; to 3 ml add a few drops of *hydrochloric acid*; the colour changes to violet. Add a few drops of *sodium hydroxide solution* until the solution is alkaline; the colour of the solution changes to brownish-yellow.

Melting range etween 213° and 218°, Appendix 5.11.

pH : Between 5.0 and 9.0, determined in a 2.5 per cent w/v solution in a mixture of 15 ml of *acetone* and 85 ml of *water*, Appendix 5.10.

Heavy metals : Not more than 10 parts per million, determined by Method B on 2.0 g, Appendix 3.2.4.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2 7.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.5 g and dissolve in 80 ml of *acetone*. Titrate with *0.1N perchloric acid* in *dioxan*, determining the end-point potentiometrically. Carry out a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.04734 g of $C_{27}H_{22}Cl_2N_4$.

Storage : Store in well-closed containers.

Clofazimine Capsules

Category : Antibacterial (leprostatic).

Dose : Clofazimine, previously untreated patients, 100 mg three times weekly; sulphone-resistant patients, 100 mg six times weekly. For the suppression of lepra reactions, 200 mg daily.

Usual strength : 100 mg.

Standards : Clofazimine Capsules contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Clofazimine, $C_{27}H_{22}Cl_2N_4$.

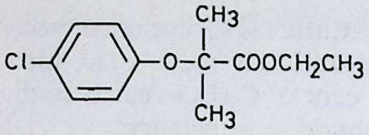
Identification : To 5 mg of the contents of a capsule add 3 ml of *chloroform* and 1 ml of *2N hydrochloric acid*; the colour of the chloroform layer changes to violet; add 2 ml of *2N sodium hydroxide*; the colour changes to brownish-yellow.

Other requirements : Comply with the requirements stated under Capsules.

Assay : Weigh accurately a quantity of the mixed contents of 20 capsules equivalent to 0.15 g of Clofazimine and dissolve in sufficient *chloroform* to produce 100.0 ml. Filter through a chloroform-washed plug of cotton wool. Dilute 5.0 ml of the clear filtrate to 100.0 ml with *chloroform*. To 5.0 ml add 5.0 ml of *0.1N methanolic hydrochloric acid* and sufficient *chloroform* to produce 50.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 490 nm, Appendix 5.15 A, using as the blank, a mixture of 5 0 ml of *0.1N methanolic hydrochloric acid* and sufficient *chloroform* to produce 50.0 ml. Calculate the content of $C_{27}H_{22}Cl_2N_4$ from the *extinction* obtained by repeating the **Assay** using *clofazimine R.S.* in place of the substance being examined, and from the declared content of $C_{27}H_{22}Cl_2N_4$ in the *clofazimine R.S.*

Storage : Store in tightly-closed containers.

Clofibrate



$C_{12}H_{15}ClO_3$ Mol. Wt. 242.70

Category : Antihyperlipidemic.

Dose : Upto 2 g daily, in divided doses.

Description : Clear, colourless to pale-yellow liquid; odour, characteristic and faintly acrid; taste, acrid at first, becoming sweet.

Solubility : Practically insoluble in *water*; soluble in *alcohol*, in *chloroform* and in *solvent ether*.

Standards : Clofibrate is ethyl 2-(4-chlorophenoxy)-2-methylpropionate.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *clofibrate R.S.*, Appendix 5.15 B.

(B) The light absorption, in the range 220 to 250 nm, of a 1-cm layer of a 0.002 per cent w/v solution, in *alcohol* exhibits a maximum only at 226 nm; *extinction* at 226 nm, about 0.455, Appendix 5.15 A.

(C) The light absorption, in the range 250 to 350 nm, of a 1-cm layer of a 0.01 per cent w/v solution, in *alcohol* exhibits two maxima, at 280 nm and 288 nm; *extinction* at 280 nm, about 0.435, and at 288 nm, about 0.31, Appendix 5.15 A.

(D) To a drop of a 10 per cent w/v solution in *solvent ether* add a drop of a saturated solution of *hydroxylammonium chloride* in *alcohol* and a drop of a saturated solution of *potassium hydroxide* in *alcohol*. Heat for two minutes on a water-bath, cool, acidify with *0.5N hydrochloric acid* and add a drop of a 1 per cent w/v solution of *ferric chloride*; a violet colour is produced.

Light absorption : *Extinction* of a 1-cm layer of a 0.001 per cent w/v solution in *alcohol* at the maximum at about 226 nm, 0.43 to 0.48, Appendix 5.15 A.

Refractive index : Between 1.500 and 1.505, determined at 20°, Appendix 5.14.

Wt. per ml : Between 1.138 and 1.144 g, determined at 20°, Appendix 5.19.

Free acid : Add 10 ml to 100 ml of *alcohol*, previously neutralised to *phenolphthalein solution* with *0.1N sodium hydroxide* and titrate with *0.1N sodium hydroxide*; not more than 0.5 ml is required.

Free phenolic bodies : Carry out the method for *gas-liquid chromatography*, Appendix 5.4.1, using the fol-

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

lowing solutions : (1) a 0.0025 per cent w/v solution of *4-chlorophenol* in *chloroform*; for solution (2) extract 10 g of the substance being examined with 20 ml of *N sodium hydroxide*, wash the lower layer with 5 ml of *water* and reserve the organic layer for the test for *volatile related substances*. Wash the alkaline layer with two quantities, each of 5 ml, of *chloroform*, discard the *chloroform* washings and acidify the alkaline layer by the dropwise addition of *hydrochloric acid*. Extract with three quantities, each of 3 ml, of *chloroform*, combine the chloroform extracts and adjust the volume to 10 ml. The chromatographic procedure may be carried out using (a) a glass column 1.5 m long and 0.4 cm in internal diameter packed with 30 per cent w/w of methyl silicone gum (SE 30 is suitable) on acid- and alkali-washing silanised diatomaceous earth (40 to 60 mesh), and maintained at 185°, (b) nitrogen as the carrier gas and (c) a flame ionisation detector. In the chromatogram obtained with solution (1) the area of the peak due to *4-chlorophenol* is greater than the area of any corresponding peak in the chromatogram obtained with solution (2).

Volatile related substances : Carry out the method for *gas-liquid chromatography*, Appendix 5.4.1, using 2 µl of each of the following solutions: For solution (1) dry the clofibrate layer reserved in the test for **Free phenolic bodies** with *anhydrous sodium sulphate* and filter; for solution (2) dilute 1 volume of solution (1) with sufficient *chloroform* to produce a solution containing 0.012 per cent w/v of the substance being examined. The chromatographic procedure may be carried out using (a) diameter packed with 30 per cent w/w of methyl silicone gum (SE 30 is suitable) on acid and alkali-washed, silanised diatomaceous earth (40 to 60 mesh) and maintained at 185°, (b) nitrogen as the carrier gas and (c) a flame ionisation detector. In the chromatogram obtained with solution (1), the total area of the peaks, except that due to the clofibrate, is not greater than ten times the area of the peak due to clofibrate in the chromatogram obtained with solution (2).

Storage : Store in tightly-closed, light-resistant containers.

Clofibrate Capsules

Category : Antihyperlipidemic.

Dose : Clofibrate, upto 2 g daily, in divided doses, in accordance with the response of the patient.

Usual strength : 0.5 g.

Standards : Clofibrate Capsules contain Clofibrate.

Uniformity of weight : Comply with the test for **Uniformity of weight** stated under Capsules. The average weight of the contents of the ten capsules is not less than 92.5 per cent and not more than 107.5 per cent of the stated weight.

Other requirements : Comply with the requirements stated under Capsules.

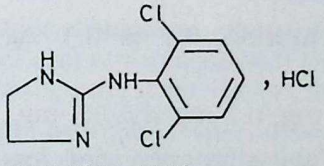
The contents of the capsules comply with the following tests:

Identification; Light absorption; Refractive index; Wt. per ml; Free phenolic bodies; Volatile related substances : Comply with the tests described under Clofibrate.

Free acidity : Add 10 ml of the contents of the capsules to 100 ml of *alcohol* previously neutralised to *phenolphthalein solution* with *0.1N sodium hydroxide* and titrate with *0.1N sodium hydroxide*; not more than 2.5 ml is required.

Storage : Store in well-closed, light-resistant containers.

Clonidine Hydrochloride



$C_9H_9Cl_2N_3, HCl$ Mol. Wt. 266.57

Category : Antihypertensive.

Dose 100 to 300 mcg daily, in divided doses.

Description : White or almost white, crystalline powder; odourless.

Solubility : Freely soluble in *water* and in *alcohol*; slightly soluble in *chloroform*; practically insoluble in *solvent ether*.

Standards : Clonidine Hydrochloride is the hydrochloride of 2-(2,6-dichloroanilino)-2-imidazoline. It contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of $C_9H_9Cl_2N_3, HCl$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *clonidine hydrochloride R.S.*, Appendix 5.15 B.

(B) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.01 per cent w/v solution exhibits a maximum at about 271 nm, Appendix 5.15 A.

(C) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

(D) The lower melting form melts at about 305° and the higher melting form melts at about 313°, Appendix 5.11.

Sulphated ash : Not more than 0.2 per cent w/w, Appendix 3.2.7.

Loss on drying : Not more than 2 per cent, determined on 0.5 g, by drying in an oven at 105° for four hours, Appendix 5.8.

Assay : Weigh accurately about 0.4 g and dissolve in 50 ml of *glacial acetic acid*. Add 10 ml of *mercuric acetate solution* and titrate with *0.05N perchloric acid*, using *1-naphtholbenzein solution* as indicator. Perform a blank titration and make any necessary correction. Each ml of *0.05N perchloric acid* is equivalent to 0.01333 g of $C_9H_9Cl_2N_3$, HCl.

Storage : Store in well-closed, light-resistant containers.

Clonidine Tablets

Category : Antihypertensive.

Dose : Clonidine Hydrochloride, 0.1 to 0.3 mg daily, in divided doses.

Usual strengths : 0.025 mg, 0.1 mg and 0.3 mg.

Standards : Clonidine Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Clonidine Hydrochloride, $C_9H_9Cl_2N_3$, HCl.

Identification : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 4 volumes of *n-butyl alcohol*, 1 volume of *acetic acid* and 3 volumes of *water* as the mobile phase. Apply separately to the plate 20 µl of each of the following two solutions: For solution (1) mix a quantity of the powdered tablets equivalent to 1 mg of Clonidine Hydrochloride with 5 ml of *water* and 5 ml of *sodium hydroxide solution* and extract with two quantities, each of 30 ml of *chloroform*. Combine the chloroform extracts and wash with 10 ml of *water*. Discard the aqueous layer, evaporate the chloroform extract to dryness. Dissolve the residue in 2.0 ml of *0.1N hydrochloric acid* with the aid of gentle heat; for solution (2) a 0.05 per cent w/v solution of *clonidine hydrochloride R.S.* After removal of the plate, allow it to dry in air and expose to iodine vapour in a closed glass tank for fifteen minutes. The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

Uniformity of content : Powder one Tablet and transfer to a separator. Add 10 ml of warm *water* and 1.0 ml of *dilute acetic acid*. Shake vigorously for five minutes and add 3.0 ml of a 0.1 per cent w/v solution of *metanil yellow*. Shake well and allow to stand for ten minutes. Extract with two successive quantities, each of 10 ml of distilled *chloroform*. Allow the two layers to separate and each time transfer the chloroform layer into another separator, taking care to ensure that no portion of the aqueous layer is transferred along with the solvent extract. Extract the combined chloroform extracts with two quantities, each of 10 ml of *N hydrochloric acid*. Discard the chloroform layer and collect the acid extracts in a flask. Make up to suitable volume with *N hydrochloric acid* to produce a solution containing 1 µg of $C_9H_9Cl_2N_3$, HCl per ml. Measure the *extinction* of a 1-cm layer at the maximum at about 530 nm, Appendix 5.15 A. Calculate the content of $C_9H_9Cl_2N_3$, HCl per tablet from the *extinction* obtained by carrying out the determination simultaneously using *clonidine hydrochloride R.S.*

Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 90 and 110 per cent of the average except that for one tablet the content may be between 85 and 115 per cent of the average.

Other requirements : Comply with the requirement stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.1 mg of Clonidine Hydrochloride into a separator, add 15 ml of warm *water*, 1 ml of *dilute acetic acid* and shake well. Add 2 ml of a 0.1 per cent w/v solution of *metanil yellow* and shake vigorously. Allow to stand for ten minutes and extract with two successive quantities, each of 40 ml of re-distilled *chloroform*. Allow the layers to separate and each time transfer the chloroform into another separator, taking care to ensure that no portion of the aqueous layer is transferred along with the solvent extract. Extract the combined chloroform extracts with two quantities, each of 40 ml of *N hydrochloric acid*. Discard the chloroform layer and collect the acid extracts in a 100-ml graduated flask. Make up to volume with *N hydrochloric acid*. Measure the *extinction* of a 1-cm layer at the maximum at about 530 nm, Appendix 5.15 A. Calculate the content of $C_9H_9Cl_2N_3$, HCl from the *extinction* obtained by carrying out the **Assay** simultaneously using *clonidine hydrochloride R.S.* and from the declared content of $C_9H_9Cl_2N_3$, HCl in the *clonidine hydrochloride R.S.*

Storage : Store in well-closed, light-resistant containers.

Clove Oil

Category : Pharmaceutical aid (flavour); local anaesthetic, used in dentistry.

Description : Colourless or pale-yellow liquid when freshly distilled, becoming darker and thicker

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

by ageing or exposure to air, odour and test those of clove.

Solubility : Freely soluble in *alcohol (70 per cent).*

Standards : Clove oil is the oil distilled from the dried flowerbuds of *Eugenia caryophyllus* (Spreng) Bull. et Harr. It contains not less than 85.0 per cent v/v of phenolic substances, chiefly eugenol, $C_{10}H_{12}O_2$.

Optical rotation : Between 0° and −1.5°, Appendix 5.12.

Wt. per ml : Between 1.038 and 1.060 g, Appendix 5.19.

Refractive index : Between 1.527 and 1.535 determined at 20°, Appendix 5.14.

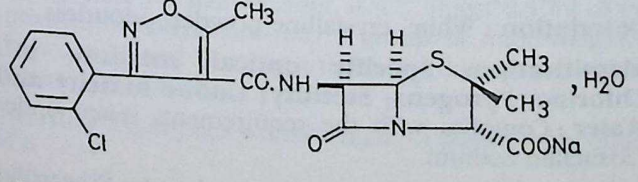
Phenol : Shake 1 ml with 20 ml of hot *water*; the water shows not more than a scarcely perceptible acid reaction with *blue litmus paper.* Cool the mixture, pass the layer of water through a wetted filter, and treat the clear filtrate with one drop of *ferric chloride-test solution.* The mixture has only a transient greyish-green colour, but not a blue or violet colour.

Heavy metals : Not more than 40 parts per million, determined on 0.5 g by Method B, Appendix 3.2.4.

Assay : Pipette 10 ml into a Cassia flask, the neck of which is graduated from 0 to 6 ml at intervals of 0.1 ml. Add 75 ml of *potassium hydroxide solution.* Shake the mixture for five minutes, and heat for ten minutes in boiling water, shaking the flask atleast three times during the heating. Cool to room temperature and when the liquids have separated completely, add sufficient *potassium hydroxide solution* to raise the lower level of the oily layer within the graduated portion of the flask. Keep aside for 18 hours and read the volume of oily layer. Not more than 1.5 ml of oil separates indicating the presence of not less than 85.0 per cent w/v of total phenolic substances.

Storage : Store in well-filled, well-closed, light-resistant containers in a cool place.

Cloxacillin Sodium



$C_{19}H_{17}ClN_3NaO_5S, H_2O$ Mol.Wt. 475.88

Category : Antibacterial.

Dose : The equivalent of 1.5 to 3 g of cloxacillin daily, in divided doses.

Description : White, crystalline powder; taste, very bitter; almost odourless; hygroscopic.

Solubility : Freely soluble in *water*, and in *alcohol*; slightly soluble in *chloroform.*

Standards : Cloxacillin Sodium is the monohydrate of sodium (6*R*)-6-[3-(2-chlorophenyl)-5-methyl-isoxazole-4-carboxamido] penicillanate. It contains not less than 95.0 per cent of $C_{19}H_{17}ClN_3NaO_5S$, calculated with reference to the anhydrous substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *cloxacillin sodium R.S.*, Appendix 5.15 B.

(B) A solution (1 in 20) gives the reactions of *sodium*, Appendix 3.1.

(C) It melts at about 178°, with decomposition, Appendix 5.11.

Specific optical rotation : Between +163° and +172°, determined at 20° in 1 per cent w/v solution, Appendix 5.12.

Light absorption : *Extinction* of a 1-cm layer of 0.01 per cent w/v solution in *0.1N hydrochloric acid*, at the maximum at about 352 nm, about 0.67, Appendix 5.15 A.

pH : Between 5.0 and 7.0, determined in a 10.0 per cent w/v solution, Appendix 5.10.

Water : Not more than 4.5 per cent w/w, Appendix 3.3.25.

Chlorine : Not less than 7.0 per cent and not more than 7.5 per cent, determined by the *oxygen-flask method*, Appendix 3.3.6, using 40 mg, and using 20.0 ml of *0.01N silver nitrate*, and *0.01N ammonium thiocyanate* in place of 10 ml of *0.05N silver nitrate*, and *0.05N ammonium thiocyanate* respectively. Each ml of *0.01N silver nitrate* is equivalent to 0.3546 mg of Cl.

Assay : Weigh accurately about 0.1 g and dissolve in sufficient *water* to produce 500.0 ml. Dilute 25.0 ml to 100.0 ml with *water.* Complete the **Assay** described under Ampicillin, beginning at the words "pipette two 2-ml aliquots of this solution...." and measuring the *extinctions* at the maximum at about 346 nm. Calculate the content of $C_{19}H_{17}ClN_3NaO_5S$ by repeating the procedure using *cloxacillin sodium R.S.* instead of the substance being examined and from the declared content of $C_{19}H_{17}ClN_3NaO_5S$ in the *cloxacillin sodium R.S.*

Cloxacillin Sodium intended for parenteral administration complies with the following additional requirements :

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using not less than 6 mg per kg of the rabbit's weight dissolved in not more than 5 ml of *water for injection.*

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Sterility : Complies with the *tests for sterility*, Appendix 4.6.

Undue toxicity : Complies with the test described under Bacitracin, using 0.5 ml of a solution containing the equivalent of 10 mg of cloxacillin per ml in *water for injection*.

Storage : Store in tightly-closed containers in a cool, dry place. If it is intended for parenteral administration, the container should be sterile and sealed so as to exclude micro-organisms.

Labelling : The label on the container states (1) the date after which the contents are not to be used; (2) the storage conditions; (3) whether or not the contents are intended for parenteral administration.

Cloxacillin Capsules

Category : Antibacterial.

Dose : The equivalent of 1.5 to 3 g of cloxacillin daily, in divided doses.

Usual strengths : The equivalent of 250 mg and 500 mg of cloxacillin.

Standards : Cloxacillin Capsules contain a quantity of Cloxacillin Sodium equivalent to not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Cloxacillin, $C_{19}H_{18}ClN_3O_5S$.

Identification : (A) Extract a quantity of the contents of the capsules equivalent to about 0.125 mg of cloxacillin with 5 ml of *water*, filter, acidify the filtrate with *dilute hydrochloric acid*, extract with 5 ml of *chloroform* and evaporate the chloroform solution to dryness without the aid of heat; the residue complies with **Identification** test (A) described under Cloxacillin Sodium.

(B) A solution (1 in 20) gives the reactions of *sodium*, Appendix, 3.1.

Other requirements : Comply with the requirements stated under Capsules.

Assay : Weigh accurately a quantity of the mixed contents of 20 capsules equivalent to 0.15 g of cloxacillin, add about 70 ml of *water*, shake for fifteen minutes; add sufficient *water* to produce 100.0 ml and filter. Dilute 2.0 ml of the filtrate to 10.0 ml with *buffered copper sulphate solution, pH 3.2*, in a stoppered test-tube, and heat in a water-bath at 70° for twenty minutes. Rapidly cool to room temperature, dilute to 20.0 ml with *alcohol* and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 338 nm, Appendix 5.15 A, using as blank an unheated buffered solution of the substance being examined, similarly diluted with alcohol. Calculate the content of $C_{19}H_{18}ClN_3O_5S$ from the *extinction* obtained by carrying out the **Assay** simultaneously using 0.160 g *cloxacillin sodium R.S.* and from the declared content of $C_{19}H_{18}ClN_3O_5S$ in the *cloxacillin sodium R.S.*

Storage : Store in tightly-closed containers in a cool place.

Labelling : The label on the container states (1) the strength in terms of the equivalent amount of cloxacillin; (2) the date after which the capsules are not intended to be used; (3) the storage conditions.

Cloxacillin Injection

Category : Antibacterial.

Dose : By intramuscular injection, the equivalent of 1.5 to 3 g of cloxacillin daily, in divided doses.

Usual strengths : The equivalent of 250 mg and 500 mg of cloxacillin.

Standards : Cloxacillin Injection is a sterile solution of Cloxacillin Sodium in Water for Injection. It is prepared by dissolving the contents of a sealed container in the requisite amount of Water for Injection immediately before use.

Content of cloxacillin, $C_{19}H_{18}ClN_3O_5S$: Determine the weight of the contents of each of ten containers as described in the test for **Uniformity of weight** under Injections. From the result of the **Assay** calculate the proportionate amount of cloxacillin, $C_{19}H_{18}ClN_3O_5S$ in each container; each mg of cloxacillin sodium, $C_{19}H_{17}ClN_3NaO_5S$ is equivalent to 0.952 mg of cloxacillin, $C_{19}H_{18}ClN_3O_5S$. This amount does not deviate from the amount stated on the label by a greater percentage than that shown in column A of the Table of Deviations, except that in the container the amount may deviate by not more than twice the percentage shown.

Other requirements : Complies with the requirements stated under Injections.

The contents of the sealed container comply with the following requirements :

Description : White, crystalline powder; odourless.

Identification; Specific optical rotation; pH; Chlorine; Pyrogens; Sterility; Undue toxicity and Water : Complies with the requirements stated under Cloxacillin Sodium.

Assay : Carry out the **Assay** described under Cloxacillin Sodium, using the mixed contents of ten containers.

Storage : Store in a cool, dry place. The constituted solution should be used within thirty minutes of preparation.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Labelling : The label on the sealed container states (1) the quantity of Cloxacillin Sodium contained in it in terms of the equivalent amount of cloxacillin; (2) the date after which the contents are not intended to be used; (3) the storage conditions.

Cobra Venom

Category : Local haemostatic.

Dose : By intramuscular injection; initial dose, 1 to 3 Mouse Units. Subsequent doses, 5 to 25 Mouse Units or more in gradually increasing doses.

Description : Almost white or very light yellow, dry powder.

Solubility : Dissolves in *water* to give a clear solution with some insoluble residue.

Standards : Cobra Venom is the dried secretion obtained from the poison gland of *Naja naja* and other species of *Naja* (Fam. Colubridae). Immediately after extraction, the poisonous secretion is dried from the frozen state. The dried venom is pooled, mixed, dissolved in ice-cold Water for Injection and then filtered through a bacteria-proof filter to give a stock solution. Further dilutions of the stock solution are made with Water for Injection under aseptic conditions to give solutions with the required number of Mouse Units per ml. These solutions are then distributed in single doses into sterile glass containers, dried from the frozen state and sealed in vacuum.

It contains not less than 50 Mouse Units per mg.

Identification : (A) A solution in *water* produces in the presence of *lecithin*, haemolysis of Red Blood Corpuscles suspended in *saline solution*.

(B) Mix the soluble fraction from at least 0.6 mg with 1 ml of *polyvalent anti-snake venom serum*, and incubate the mixture for half an hour at 37°. Inject 0.5 ml of the mixture intravenously into a group of mice weighing between 17 and 20 g; no animal dies during twenty-four hours of observation.

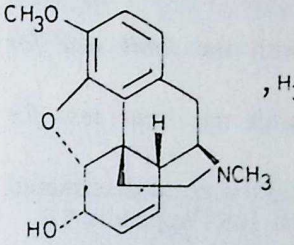
Sterility : Complies with the *tests for sterility*, Appendix 4.6.

Assay : Carry out the *biological assay of snake venom*, Appendix 2.33, and express the result in terms of number of Mouse Units per mg.

Storage : Store in single-dose, light-resistant containers.

Labelling : The label on the container states (1) the number of Mouse Units per container; (2) the volume of Water for Injection to be used for reconstitution.

Codeine Phosphate



$, H_3PO_4 , \frac{1}{2} H_2O$

$C_{18}H_{21}NO_3.H_3PO_4.\frac{1}{2}H_2O$ Mol. Wt. 406.37

Category : Analgesic, antitussive.

Dose : 10 to 60 mg.

Description : Fine, white, needle-shaped crystals, or hexagonal prisms, or a white crystalline powder; odourless; taste, bitter. It changes colour on exposure to light.

Solubility : Freely soluble in *water*; slightly soluble in *alcohol (90 per cent)*; sparingly soluble in *chloroform* and in *solvent ether*.

Standards : Codeine Phosphate is hemihydrate of the dihydrogen phosphate of 7,8-didehydro-4,5-epoxy-3-methoxy-17-methylmorphinan-6-ol. It contains not less than 98.0 per cent and not more than the equivalent of 100.5 per cent of $C_{18}H_{21}NO_3.H_3PO_4$, calculated with reference to the dried substance.

Identification : (A) On the surface of one drop of *nitric acid*, place a little of the powder; a yellow, but not red, colour is produced (distinction from morphine).

(B) Dissolve 0.1 g in 1 ml of *sulphuric acid*, and 1 drop of *ferric chloride test-solution*, or of *ammonium molybdate solution* and warm gently, a bluish-violet colour is produced; add a drop of *dilute nitric acid*; the colour changes to red.

(C) A solution (1 in 20) gives the reactions of *phosphates*, Appendix 3.1.

Specific optical rotation : Between −98° and −102°, determined in a 2.0 per cent w/v solution, Appendix 5.12.

pH : Between 4.2 and 5.0, determined in a 4.0 per cent w/v solution, Appendix 5.10.

Clarity and colour of solution : A 4.0 per cent w/v solution is clear and not more intensely coloured than a

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

mixture of 1.2 ml of *ferric chloride C.S.*, 0.3 ml of *cobalt chloride C.S.* and sufficient *hydrochloric acid (1 per cent w/v HCl)* to produce 100 ml.

Morphine : To 5 ml of a 2.0 per cent w/v solution in *0.1N hydrochloric acid* add 2 ml of 1 per cent w/v solution of *sodium nitrite*, set aside for fifteen minutes and add 3 ml of *dilute ammonia solution*; the yellow colour of the solution is not deeper than that obtained when 5 ml of a 0.0025 per cent w/v solution of *morphine hydrochloride* in *0.1N hydrochloric acid* is treated in the same manner.

Chlorides : 0.5 g complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphates : 0.5 g complies with the *limit test for sulphates*, Appendix 3.2.8.

Loss on drying : Not more than 3.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.4 g and dissolve in 30 ml of *glacial acetic acid*. Add few drops of *crystal-violet solution* and titrate with *0.1N perchloric acid*. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.03974 g of $C_{18}H_{21}NO_3,H_3PO_4$.

Storage : Store in well-closed containers.

Codeine Phosphate Syrup

Codeine Syrup

Category : Analgesic; antitussive.

Dose : Codeine Phosphate, 10 to 40 mg.

Standards : Codeine Phosphate Syrup contains not less than 0.48 per cent and not more than 0.52 per cent w/v of Codeine Phosphate, $C_{18}H_{21}NO_3,H_3PO_4,\frac{1}{2}H_2O$.

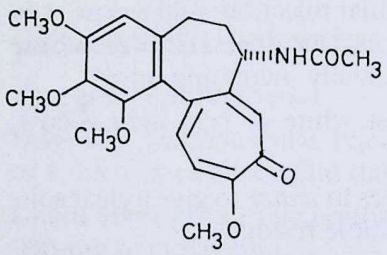
Identification : To 10 ml add sufficient *dilute ammonia solution* until the solution is alkaline and extract with three quantities, each of 10 ml, of *chloroform*. Evaporate the combined chloroform extracts to dryness on a water-bath and dry the residue at 80°. The residue complies with **Identification** tests (A) and (B) described under Codeine Phosphate.

Assay : Weigh accurately about 10 g, add *dilute ammonia solution* until the solution is alkaline to *litmus paper* and extract with four quantities, each of 25 ml of *chloroform*. Wash each extract successively with the same 10 ml of *water*; bulk the chloroform extracts and evaporate off the chloroform. To the residue add 5 ml of *alcohol* and again evaporate. Dissolve the residue in 5.0 ml of *0.05N hydrochloric acid* and titrate the excess of acid with *0.05N sodium hydroxide*, using *methyl red solution* as indicator. Each ml of *0.05N hydrochloric acid* is equivalent to 0.02032 g of $C_{18}H_{21}NO_3,H_3PO\frac{1}{2}H_2O$.

Determine the weight per ml of the syrup and calculate the percentage w/v of codeine phosphate in the syrup

Storage : Store in tightly-closed, light-resistant containers.

Colchicine



$C_{22}H_{25}NO_6$ Mol. Wt. 399.44

Category : Gout suppressant.

Dose : Initial dose, 1 mg; subsequent doses, 0.5 mg every two hours.

Description : Pale-yellow crystals, amorphous scales, or powder; odourless.

CAUTION—It is extremely poisonous.

Solubility : Freely soluble in *water*, but moderately concentrated solutions may deposit crystals of a sesquihydrate, which is slightly soluble in cold *water*; slightly soluble in *solvent ether*; freely soluble in *alcohol* and in *chloroform*.

Standards : Colchicine is an alkaloid, (*S*)-*N*-(5,6,7,9-tetrahydro-1,2,3,10-tetramethoxy-9-oxobenzo[*a*]-heptalen-7-yl) acetamide, obtained from various species of *Colchicum*. It contains not less than 97.0 per cent and not more than the equivalent of 103.0 per cent of $C_{22}H_{25}NO_6$, calculated with reference to the anhydrous, solvent free substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *colchicine R.S.*, Appendix 5.15 B.

(B) The light absorption, in the range 230 to 400 nm, of a 1-cm layer of a 0.001 per cent w/v solution in *alcohol* exhibits two maxima, at 243 nm and 350 nm; *extinction* at 243 nm, about 0.73 and at 350 nm, about 0.42, Appendix 5.15 A.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

(C) Dissolve 50 mg in 1.5 ml of *water*; a yellow solution is produced; the colour is intensified on adding mineral acids.

(D) Mix 1 mg with 0.2 ml of *sulphuric acid* in a white dish; a yellow colour is produced; add 0.05 ml of *nitric acid*, the colour changes to greenish-blue and then reddish and finally yellow or almost colourless; add an excess of *5N sodium hydroxide*, the colour changes to red.

Specific optical rotation : Between −425° and −450°, determined in a 1.0 per cent w/v solution, Appendix 5.12.

Colchiceine : To 5 ml of a 1.0 per cent w/v solution add 0.1 ml of a 10.5 per cent w/v solution of *ferric chloride*; any colour produced is not more intense than that obtained with a mixture of 2.0 ml of *ferric chloride C.S.*, 1.0 ml of *cobalt chloride C.S.*, and 2 ml of *copper sulphate C.S.*, Appendix 7.2.

Solvent : Carry out the method for *gas-liquid chromatography*, Appendix 5.4.1, using the following solutions in *water* containing (1) 0.1 per cent v/v of *alcohol-free chloroform*, 0.1 per cent v/v of *ethyl acetate*, and either 0.1 per cent v/v (for the determination of ethyl acetate) or 0.02 per cent v/v (for the determination of chloroform) of *ethyl alcohol* (internal standard); (2) 1.0 per cent w/v of the dried substance being examined; and (3) 1.0 per cent w/v of the dried substance being examined and the same concentration of the internal standard as in solution (1). The chromatographic procedure may be carried out using (a) a column 1.5 m long and 0.4 cm in internal diameter packed with 10 per cent w/w of macrogol 1000 supported on white diatomaceous earth (100 to 120 mesh), maintained at 75°, (b) *nitrogen* as the carrier gas, and (c) a flame ionisation detector. Calculate the percentage w/w of ethyl acetate or chloroform, assuming the *weight per ml*, at 25°, to be 0.901 g or 1.477 g, respectively.

The sum of the content of chloroform or ethyl acetate and of water (determined in the test below) is not more than 10 per cent.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using a suitable aluminium oxide containing a substance that fluoresces at about 254 nm as the coating substance and a mixture of 25 volumes of *chloroform*, 20 volumes of *acetone*, and 0.4 volume of *strong ammonia solution* as the mobile phase. Apply separately to the plate 2 µl of each of two solutions in *alcohol* containing (1) 5 per cent w/v of the substance being examined and (2) 0.25 per cent w/v of the substance being examined. After removal of the plate allow it to dry in air and examine under an ultra-violet lamp having a maximum output at above 254 nm. Any spot in the chromatogram obtained with solution (1), other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (2).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Water : Not more than 3.0 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately about 0.05 g and dissolve in a mixture of 10 ml of *acetic anhydride* and 20 ml of *toluene*. Titrate with *0.02N perchloric acid* determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.02N perchloric acid* is equivalent to 0.007988 g of $C_{22}H_{25}NO_6$.

Storage : Store in tightly-closed, light-resistant containers.

Corticotrophin

Adrenocorticotrophin Hormone; ACTH

Category : Adrenocortical steroid (anti-inflammatory); diagnostic aid (adrenocortical insufficiency).

Dose : By intravenous or intramuscular injection, 40 Units to 80 Units a day.

Description : White or practically white, amorphous solid or flakes. Hygroscopic.

Standards : Corticotrophin is a substance obtained from the anterior lobe of the pituitary gland of the ox or the pig and contains the corticotrophic principle which increases the rate at which corticoid hormones are secreted by the adrenal glands.

The method of preparation used should avoid, as far as possible, hydrolysis or other degradation of the active principles.The purified material may be suitably sterilised and dried.

It contains not less than 25 Units per mg (ox material) or not less than 45 Units per mg (pig material). It may contain a suitable antimicrobial agent.

Clarity of solution : A 1.0 per cent w/v solution is clear or not more than slightly opalescent.

pH : Between 3.0 and 5.0, determined in a 1.0 per cent w/v solution, Appendix 5.10.

Pressor activity : Not more than 5 Units per 100 Units of corticotrophic activity, determined by the *biological assay of vasopressin injection*, Appendix 2.13.

Undue toxicity : Complies with the *test for undue toxicity*, Appendix 2.37, using a volume equivalent to 5 Units dissolved in 0.5 ml of *saline solution* and extending the observation period to 48 hours.

Sterility : Complies with the *tests for sterility*, Appendix 4.6.

Loss on drying : Not more than 7.0 per cent, deter-

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

mined on 1.0 g by drying "in vacuo at 60°", Appendix 5.8.

Assay : Carry out the *biological assay of corticotrophin*, Appendix 2.8. The estimated potency determined by either method is not less than 80 per cent and not more than 125 per cent of the stated potency. The fiducial limits of error of the estimated potency are not less than 64 per cent and not more than 156 per cent of the stated potency

Storage : Store in well-closed, light-resistant containers, in a cool place.

Labelling : The label on the container states (1) the animal source of the material; (2) the number of Units per mg; (3) the route or routes of injection used in determining the potency; (4) the storage conditions; (5) the date after which it is not intended to be used.

Corticotrophin Injection

ACTH Injection

Category : Adrenocortical steroid (anti-inflammatory); diagnostic aid (adrenocortical insufficiency)

Dose : Intravenous use (using material labelled "For intravenous use only"). For maximal adrenal stimulation, 15 to 30 Units, according to the age of the patient, by slow infusion over eight to twenty-four hours.

Subcutaneous or intramuscular use (using material labelled "For subcutaneous or intramuscular use only"). The dose is determined by the physician in accordance with the needs of the patient.

Standards : Corticotrophin Injection is a sterile solution of Corticotrophin in Water for Injection. It is prepared by dissolving the contents of a sealed sterile container in the requisite amount of Water for Injection, immediately before use. The sealed container may contain added inert substances, provided they do not interfere with the assay.

The contents of the sealed container comply with the requirements for **Clarity of solution, pH, Pressor activity, Undue toxicity, Sterility, Loss on drying and Assay**, described under Corticotrophin.

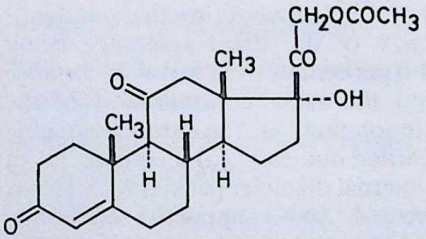
Uniformity of weight : Determine the weight of the contents of each of ten containers as described in Test (1) under **Uniformity of weight**, under Injection. Calculate the average weight of the contents. The weight of the contents of each container does not deviate from the average weight by more than 10 per cent, except that in one container the weight may deviate by not more than 20 per cent.

Other requirements : Comply with the requirements stated under Injections.

Storage : Store in sealed containers of light-resistant glass, in a cool place.

Labelling : The label on the sealed container states (1) the total number of Units in the container; (2) either (a) "For intravenous use only" or (b) "For subcutaneous or intramuscular use only"; (3) the nature and quantity of the liquid to be added for reconstitution; (4) the animal source of the contents; (5) the name of any added substances; (6) the storage conditions; (7) the date after which the contents are not intended to be used.

Cortisone Acetate



$C_{23}H_{30}O_6$ Mol. Wt. 402.49

Category : Adrenocortical steroid (anti-inflammatory).

Dose : By intramuscular injection, 50 to 400 mg. For replacement therapy, 12.5 to 50 mg daily, in divided doses.

Description : White or creamy-white crystals or crystalline powder; odourless.

Solubility : Insoluble in *water*; slightly soluble in *alcohol* and in *solvent ether*; sparingly soluble in *acetone*; soluble in *chloroform* and in *dioxan*.

Standards : Cortisone Acetate is 17α,21-dihydroxypregn-4-ene, 3, 11, 20-trione 21-acetate. It contains not less than 96.0 per cent and not more than the equivalent of 104.0 per cent of $C_{23}H_{30}O_6$, calculated with reference to the dried substance.

Identification : (A) Complies with the test for *identification of steroids*, Appendix 3.3.11, using *solvent I* and *mobile phase A*. and applying to the plate. 2 µl of each of the solutions.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

(B) Dissolve 1 mg in 2 ml of *sulphuric acid*; a yellowish-green colour is produced which becomes yellowish-orange. Set aside the solution for five minutes and expose to ultra-violet light; it exhibits a pale-yellow fluorescence (distinction from prednisone).

(C) To 50 mg add 2 ml of *alcoholic potassium hydroxide solution* and heat in a boiling water-bath for five minutes. Cool, add 6 ml of mixture of 1 volume of *sulphuric acid* diluted to 3.5 volumes with *water* and boil gently for one minute; the odour of ethyl acetate is perceptible.

Light absorption : *Extinction* of a 1-cm layer of a 0.001 per cent w/v solution in *aldehyde-free ethyl alcohol* at the maximum at about 240 nm, between 0.38 and 0.40, Appendix 5.15 A.

Specific optical rotation : Between +209° and +217°, determined in a 1.0 per cent w/v solution in *dioxan*, Appendix 5.12.

Related foreign steroids : Complies with the test for *related foreign steroids, Method B*, Appendix 3.3.12.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 0.5 g by drying in an oven at 105°, Appendix 5.8.

Assay : Carry out the **Assay** described under Betamethasone, using *cortisone acetate R.S.* for preparing the *standard solution.*

Storage : Store in well-closed, light-resistant containers.

Cortisone Injection

Cortisone Acetate Injection

Category : Adrenocortical steroid (anti-inflammatory).

Dose : Cortisone Acetate. By intramuscular injection, 50 to 400 mg daily, in single or divided doses.

Usual strength : 25 mg per ml.

Description : White suspension which settles on standing but readily disperses on shaking.

Standards : Cortisone Injection is a sterile suspension of a very fine powder of Cortisone Acetate in Sodium Chloride Injection, containing suitable dispersing agents. It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of $C_{23}H_{30}O_6$.

Identification : Extract a volume equivalent to 30 mg of Cortisone Acetate with 6 ml of *chloroform*. The residue obtained after removal of the chloroform complies with **Identification** tests (A) to (C) described under Cortisone Acetate.

pH : Between 5.0 and 7.2, Appendix 5.10.

Other requirements : Complies with the requirements stated under Injections.

Assay : Transfer to a separator an accurately measured volume equivalent to 20 mg of Cortisone Acetate and dilute with *water* to about 15 ml. Extract with four quantities, each of 20 ml, of *chloroform*, filtering each portion through chloroform-washed cotton into a 100-ml volumetric flask. Add *chloroform* to volume and mix. Transfer 10.0 ml of the solution into a 100-ml volumetric flask, add *chloroform* to volume, and mix. Transfer 10.0 ml of the resulting solution into a glass-stoppered 50-ml flask, evaporate the chloroform on a water-bath just to dryness, cool, and dissolve the residue in 20.0 ml of *aldehyde-free ethyl alcohol* to give the *test solution.* Carry out the *assay of steroids*, Appendix 3.3.10, using *cortisone acetate R.S.* to prepare the *standard solution.*

Storage : Store in single-dose or multiple-dose, light-resistant containers, in a cool place. It should not be allowed to freeze.

Labelling : The label on the container states (1) the names of the dispersing agents; (2) "Not to be given by intravenous injection"; (3) that the container should be gently shaken before a dose is withdrawn.

Cortisone Tablets

Category : Adrenocortical steroid (anti-inflammatory).

Dose : Cortisone Acetate, 12.5 to 50 mg daily, in divided doses.

Usual strengths : 5 mg; 25 mg.

Standards : Cortisone Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Cortisone Acetate, $C_{23}H_{30}O_6$.

Identification : Extract a quantity of the powdered tablets equivalent to 0.1 g of Cortisone Acetate with 5 ml of *chloroform* and remove the chloroform from the extract; the residue complies with the test for *identification of steroids*, Appendix 3.3.11, using *solvent I* and *mobile phase B*.

Other requirements : Comply with the requirements stated under Tablets.

Uniformity of content(for 5 mg tablets) : Powder one tablet, add 50 ml of *ethyl alcohol*, shake for thirty minutes and add sufficient *ethyl alcohol* to produce 100.0 ml.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Centrifuge and pipette a suitable volume of the supernatant liquid equivalent to 0.5 mg of Cortisone Acetate and dilute to 50.0 ml with *ethyl alcohol*. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 240 nm, Appendix 5.15 A. Calculate the content of $C_{23}H_{30}O_6$, taking 390 as the value of E(1 per cent, 1-cm) at the maximum at about 240 nm.

Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 90 and 110 per cent of the average except that for one tablet the content may be between 85 and 115 per cent of the average.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 2.5 mg of Cortisone Acetate and transfer with the aid of *water* to a separator. Extract with four quantities, each of 20 ml, of *chloroform*, filtering each extract through chloroform-washed cotton wool into a 250-ml volumetric flask. Add *chloroform* to volume and mix. Transfer 20.0 ml of this solution to a glass-stoppered 50-ml flask, evaporate the chloroform just to dryness on a water-bath. Cool and dissolve the residue in 20.0 ml of *aldehyde-free ethyl alcohol* to give the *test solution*. Carry out the *assay of steroids*, Appendix 3.3.10, using *cortisone acetate R.S.* for preparing the *standard solution*.

Storage : Store in well-closed, light-resistant containers.

Absorbent Cotton Wool

Absorbent Cotton

Category : Surgical dressing.

Standards : Absorbent cotton wool consists of the trichomes or good quality new combers obtained from the seed coat of various species of the genus *Gossypium* Linn., cleaned, purified and bleached. It does not contain any colouring matter.

Description : White, carded fibres of average staple length not less than 10 mm, containing not more than traces of leaf residue, seed coat and other impurities. It offers appreciable resistance when pulled and does not shed a significant quantity of dust when shaken gently; odourless.

Identification : (A) Treat with *iodinated zinc chloride solution*; the fibres become violet.

(B) When examined under a microscope, each fibre is seen to consist of a single cell, upto 4 cm long and upto 40 µm wide, in the form of a flattened tube with thick and rounded matter and often twisted. Not more than an occasional isolated foreign fibre is seen.

Acidity or Alkalinity : To 15 g add 150 ml of *water*, macerate for two hours in a dosed vessel, decant the liquid, carefully squeezing out the residual liquid with a glass rod and mix. Reserve 10 ml for the test for **Surface-active substances** and filter the remainder.

To 25 ml of the filtered extract add 0.1 ml of dilute *phenolphthalein solution*; to another 25 ml add 0.05 ml of *methyl orange solution*. Neither solution shows a pink colour.

Surface-active substances : Into a 25-ml graduated, ground-glass stoppered cylinder with external diameter of 18 to 22 mm, previously rinsed with *sulphuric acid* and then with *water*, add the portion of the extract reserved in the previous test, shake vigorously 30 times in ten seconds, allow to stand for one minute and shake again 30 times. After five minutes, the height of the froth does not exceed 2 mm above the surface of the liquid.

Neps : A thin layer approximately equivalent to 0.5 g for an area of 450 sq cm spread uniformly between two clear glass plates, and viewed by the naked eye under transmitted light, does not show more neps than about an average of 250 for three tests.

Absorbency : Carry out the *tests for absorbency*, Appendix 5.1.

Fluorescence : Examine a layer about 5 mm in thickness under an ultra-violet lamp having a maximum output at 365 nm. It shows only a slight brownish-violet fluorescence and a few yellow particles; not more than a few isolated fibres show an intense blue fluorescence.

Colouring matter : Slowly extract 10 g in a narrow percolator with *alcohol* until 50 ml of extract is obtained, pour the liquid into a colourless glass cylinder and examine a 20-cm layer against a white background. A very faint yellow tinge may be observed but no bluish or greenish tinge is apparent.

Water soluble substances : Not more than 0.5 per cent, determined by the following method : Boil 5 g with 500 ml of *water* for thirty minutes, stirring frequently, and replace the water lost by evaporation. Decant the liquid into a beaker, squeeze the residual liquid from the material carefully with a glass rod, mix the liquids and filter the extract whilst hot. Evaporate 400 ml and dry the residue to constant weight at 105°.

Ether soluble substances : Not more than 0.5 per cent, determined by the following method : Extract 5 g with *solvent ether* in a continuous extraction apparatus such as a Soxhlet apparatus for four hours, in such a way that the rate is at least four extractions per hour. Evaporate the ether extract and dry the residue to constant weight at 105°.

Sulphated ash : Not more than 0.5 per cent, Appendix 3.2.7.

Loss on drying : Not more than 8.0 per cent, determined on 5.0 g by drying in an oven at 105°, Appendix 5.8.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Packaging : Package in rolls of not more than 500 g of a continuous lap, with a light-weight paper running under the entire lap, the paper being of such width that it may be folded over the edges of the lap, the two together being tightly and evenly rolled, and enclosed and sealed in a well-closed container.

Cresol

Category : Disinfectant, pharmaceutical aid.

Description : Almost colourless to pale brownish-yellow liquid, becoming darker on keeping or on exposure to light; odour, resembling that of phenol, but more tarry; taste of an aqueous solution, pungent.

Solubility : Soluble in *water*, usually forming a cloudy solution, miscible with *alcohol*, with *chloroform*, with *solvent ether*, with *glycerin* and with fixed and volatile oils.

Standards : Cresol is a mixture of cresols and other phenols obtained from coal tar.

Identification : To 0.5 ml add 300 ml of *water*, shake and filter. Divide the filtrate into two parts:

(1) To one part add *ferric chloride test-solution*; a transient bluish colour is produced.

(2) To the other part add *bromine solution*; a pale yellow flocculent precipitate is produced.

Distillation-range : Not more than 2.0 per cent v/v distils below 188°, and not less than 80.0 per cent v/v between 195° and 205°, Appendix 5.3.

Acidity : A 2 per cent w/v solution is neutral to *bromocresol purple solution*.

Wt. per ml : Between 1.030 and 1.038 g, Appendix 5.19.

Hydrocarbons and Volatile bases : Place 50 ml in a 500-ml round-bottomed flask, add about 83 ml of a 27 per cent w/v solution of *sodium hydroxide*, and 100 ml of *water*, and mix thoroughly. Connect the flask to a splash-bulb and air condenser about 60 cm long, with the end of the air-condenser fitting closely into the neck of a 250-ml pear-shaped separator and passing well within the separator, which has a cylindrical graduated portion above the stopcock. Fill the graduated portion of the separator with *water*. Distil rapidly until 75 ml of distillate has been collected, cooling the separator in running *water*, if necessary. Allow the separator to stand in a vertical position until separation is complete and draw off the aqueous liquid into a titration flask.

Hydrocarbons—Allow the separator to stand for a short time, measure the volume of hydrocarbon oil in the graduated portion and warm if necessary in order to keep the oil in the liquid state; subtract volume of volatile bases in the hydrocarbon oil, as determined in the following test; not more than 0.5 per cent v/v of hydrocarbon oil is present.

Volatile bases—To the aqueous portion of the distillate, obtained in the preceding test, add any aqueous liquid still remaining in the separator and neutralise it if necessary with *0.1N hydrochloric acid*, using *phenolphthalein solution* as indicator. Titrate with *N hydrochloric acid*, using *methyl orange solution* as indicator. Wash the oil from the separator into the titration flask with *water* and again titrate with *N hydrochloric acid*. From the volume of additional *N hydrochloric acid* calculate the proportion of volatile bases in the hydrocarbon oil. From the total volume of *N hydrochloric acid* used in both titrations calculate the proportion of volatile bases in the cresol; each ml of *N hydrochloric acid* is equivalent to 0.08 ml of volatile bases; not more than 0.1 per cent v/v of volatile bases, calculated as pyridine, are present.

Sulphur compounds : Place about 20 ml in a small conical flask. Moisten a piece of filter paper with a 10 per cent w/v solution of *lead acetate* and fix it on the mouth of the flask; heat the flask on a water-bath for five minutes; the filter paper shows not more than a light yellow colour.

Non-volatile matter : Not more than 0.1 per cent w/v, when evaporated on a water-bath and dried to constant weight at 105°

Storage : Store in well-closed, light-resistant containers.

Cresol With Soap Solution

Lysol

Category : Disinfectant.

Description : Amber-coloured to reddish-brown liquid; odour, that of cresol; soapy to touch.

Solubility : Miscible up to 10 per cent v/v with *water* and in all proportions with *alcohol*. 5 ml mixed with 95 ml of a *water* forms a clear solution without producing any opalescence on standing for 3 hours.

Standards : Cresol with Soap Solution is prepared by the saponification of a mixture of Cresol with vegetable oils or the mixed fatty acid derived therefrom, excluding coconut and palm kernel oils. The vegetable oils may be cottonseed, linseed, or soyabean or similar oils. It contains not less than 47.0 per cent and not more than 53.0 per cent v/v of Cresol.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Alkalinity : Dilute 5 ml with 50 ml of *alcohol* neutralised to *phenol red solution*, and titrate with *N sulphuric acid*, using *phenol red solution* as indicator; not more than 0.6 ml is required.

Hydrocarbons and Volatile bases : Distil 120 ml until all the water and 50 ml of cresol have been collected. The cresol thus recovered complies with the test for Hydrocarbons and Volatile bases described under Cresol. In doing these tests the aqueous portion of the distillate is used instead of an equal volume of water.

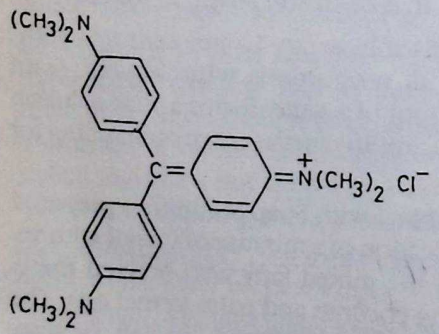
Sulphur compounds : Complies with the test for sulphur compounds described under Cresol.

Assay : To 50 ml add 150 ml of *kerosene*, mix and add little powdered *pumice stone* and 3 g of *sodium bicarbonate*. Distil into a separator, the rate of distillation being not more than two drops per second until the kerosene and cresol have completely distilled. This is indicated by the distillate being yellow in colour. Stop the distillation, add 50 ml of *kerosene*, and collect a further 50 ml of the distillate. Discard the lower aqueous layer in the separator, dry the remainder with *anhydrous calcium chloride* and shake with 10 ml of *sulphuric acid (50 per cent w/w)*. Set aside for two hours, reject the acid layer and to the kerosene layer add 40 ml of *sodium hydroxide solution* and shake for five minutes. Transfer the alkaline layer to a 100-ml graduated flask and extract the kerosene layer with 20 ml of *sodium hydroxide solution* adding the alkaline layer to that in the 100-ml graduated flask. Add *sodium hydroxide solution* from a burette to make the volume in the flask to 100 ml. The difference between the burette reading and 40.5 is equal to the volume of cresol in 50 ml of the sample.

Storage : Store in well-closed, light-resistant containers.

Crystal Violet

Gentian Violet



$C_{25}H_{30}ClN_3$ Mol.Wt. 407.99

Category : Antiseptic.

Description : Dark green powder or greenish glistening pieces having a metallic lustre; odourless or has a faint odour.

Solubility : Slightly soluble in *water*; soluble in *chloroform*, in *alcohol* and in *glycerin*; practically insoluble in *solvent ether*.

Standards: Crystal Violet consists mainly of 4-[4,4'-bis-(dimethylamino)-benzhydrylidene] cyclohexa-2,5-dien-1-ylidenedimethylammonium chloride (hexamethylpararosaniline chloride) and small amounts of the chlorides of pentamethylpararosaniline and tetramethylpararosaniline. It contains not less than 93.0 per cent of hexamethylpararosaniline, $C_{25}H_{30}ClN_3$, calculated with reference to the dried substance.

Identification : (A) Sprinkle about 1 mg on 1 ml of *sulphuric acid*; it dissolves giving an orange or brownish-red colour. On diluting cautiously with *water*, the colour at first changes to brown, then to green and finally to blue.

(B) To 10 ml of a 0.2 per cent w/v solution add about 0.25 ml of *hydrochloric acid*. Add drop by drop *tannic acid solution*; a deep blue precipitate is produced.

Related substances : Carry out in subdued light the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 100 volumes of *n-butanol*, 12 volumes of *acetic acid* and 2 volumes of *water* as the mobile phase. Apply separately to the plate 5 µl of each of three freshly prepared solutions in *methyl alcohol* containing (1) 0.025 per cent w/v of the substance being examined; (2) 0.025 per cent w/v of *crystal-violet R.S.* and (3) 0.001 per cent w/v of the substance being examined. After removal of the plate, allow it to dry in air and examine it. The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2). Any spot in the chromatogram obtained with solution (1), other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (3)

Arsenic : Not more than 10 parts per million, Appendix 3.2.1.

Zinc : Moisten 0.1 g with *sulphuric acid* and ignite. Boil the residue with 5 ml of *dilute hydrochloric acid*, 0.15 ml of *nitric acid* and 5 ml of *water*. Add 5 ml of *dilute ammonia solution* and boil. Filter and to the filtrate add 0.1 ml of *ammonium sulphide solution*; no turbidity or white precipitate is produced.

Heavy metals : Not more than 20 parts per million, determined by Method A, Appendix 3.2.4, on a solution prepared in the following manner: Moisten 1 g with a few drops of *water*, add 3 ml of *sulphuric acid* and 2 ml of *nitric acid*. When the violent reaction subsides, heat until no brown fumes are evolved. Add further quantities of

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

nitric acid, 3 ml at a time, until a pale-yellow liquid is obtained. Add 2 ml of *perchloric acid* gradually, with caution. When the violent reaction subsides, heat with further small quantities of *nitric acid* as before till a colourless solution is obtained. If the solution is not colourless, add a further 2 ml of *perchloric acid* and continue adding *nitric acid* until the solution becomes colourless. Boil for fifteen minutes and cool. Make the solution just alkaline with *dilute ammonia solution*. Add dropwise *dilute acetic acid* till slightly acid to *litmus* and then add 2 ml of *dilute acetic acid* in excess. Filter if necessary and adjust the volume to 25 ml with *water*.

Alcohol-insoluble matter : Weigh accurately about 1 g and boil with 50 ml of *alcohol (90 per cent)* under a reflux condenser for fifteen minutes. Filter, wash the residue on the filter with hot *alcohol (90 per cent)* until the washings cease to be coloured violet. Dry to constant weight at 105°; the residue weighs not more than 10 mg.

Sulphated ash : Not more than 3.0 per cent, Appendix 3.2.7.

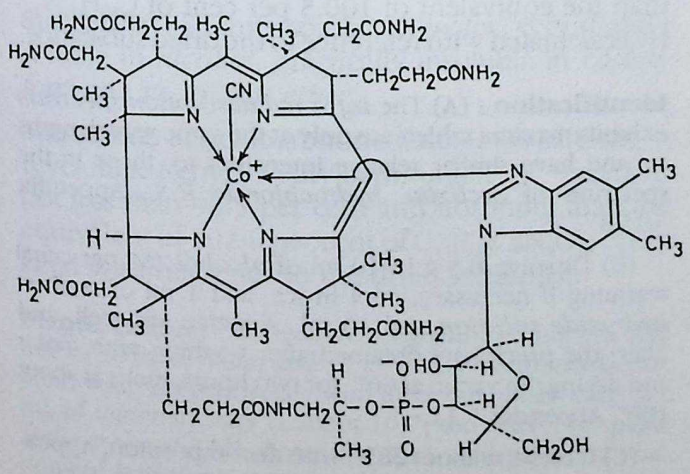
Loss on drying : Not more than 9.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.1 g and dissolve in sufficient *water* to produce 1000.0 ml. Dilute 20.0 ml to 250.0 ml with *water*. Carry out the *microbiological assay of crystal-violet*, Appendix 4.4.

Storage : Store in well-closed containers.

Cyanocobalamin

Vitamin B_{12}



$C_{63}H_{88}CoN_{14}O_{14}P$ Mol. Wt. 1355.38

Category : B group Vitamin; haematopoietic.

Dose : In the treatment of megaloblastic anaemia, by intramuscular injection, 1 to 2 mg, in divided doses, in the first week. Subsequent doses, 250 micrograms weekly until the blood count is normal, maintenance dose, 250 micrograms every three or four weeks.

Description : Dark red crystalline powder; odourless; tasteless. Very hygroscopic.

Solubility : Sparingly soluble in *water*; practically insoluble in *chloroform* and in *solvent ether*; soluble in *alcohol*.

Standards : Cyanocobalamin is Coα-[α-(5,6-dimethylbenzimidazolyl)]-Co β-cyanocobamide. It contains not less than 96.0 per cent and not more than the equivalent of 100.5 per cent of $C_{63}H_{88}CoN_{14}O_{14}P$, calculated with reference to the dried substance.

Identification : (A) Dissolve 2.0 mg in sufficient *water* to produce 50.0 ml and measure the *extinctions* of the solution at 278, 361 and 550 nm, Appendix 5.15 A. The ratio of the *extinction* at 361 nm to that at 278 nm is between 1.70 and 1.88 and the ratio of the *extinction* at 361 nm to that at 550 nm is between 3.15 and 3.45.

(B) Mix about 1 mg with 10 mg of *potassium sulphate* and 0.1 ml of *N sulphuric acid* and heat carefully to redness. Allow to cool, add to the residue 0.1 ml of *water*, 0.5 ml of a saturated solution of *ammonium thiocyanate* and 0.5 ml of *benzyl alcohol* and shake; a blue colour is formed and is taken into the benzyl alcohol layer.

Pseudo-cyanocobalamin : Dissolve 1.0 mg in 20 ml of *water* and transfer the solution to a small separator. Add a mixture of 2.5 ml of *carbon tetrachloride* and 2.5 ml of *cresol* and shake well for one minute. Allow to separate, draw off the lower layer into a second separator, add 7 ml of *dilute sulphuric acid*, shake well and allow to separate completely, centrifuging, if necessary; the separated upper layer is colourless or has no more colour than a mixture of 0.15 ml of *0.1N potassium permanganate* and 250 ml of *water*.

Coloured impurities : Not more than 4.0 per cent, determined by the following method: Dissolve 5.0 mg in the minimum quantity of *water* and carry out the test for **Coloured impurities** described under Hydroxocobalamin.

Loss on drying : Not more than 12.0 per cent, determined on 20 mg by drying in an oven at 105°, Appendix 5.8.

Assay : Protect the solution from light throughout the assay.

Weigh accurately about 25 mg and dissolve in sufficient *water* to produce 1000.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 361 nm, Appendix 5.15 A. Calculate the content of $C_{63}H_{88}CoN_{14}O_{14}P$, taking 207 as the value of E(1 per cent, 1-cm), at the maximum at about 361 nm.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Storage : Store in tightly-closed, light-resistant containers.

Cyanocobalamin Injection

Vitamin B_{12} Injection

Category : B group Vitamin; haematopoietic.

Dose : Cyanocobalamin, in the treatment of megaloblastic anaemia, by intramuscular injection, 1 to 2 mg, in divided doses, in the first week; subsequent doses, 250 micrograms weekly until the blood count is normal; maintenance dose, 250 micrograms every three or four weeks. If the nervous system is involved the doses should be increased.

Usual strengths : 100 micrograms per ml; 500 micrograms per ml; 1000 micrograms per ml.

Standards : Cyanocobalamin Injection is a sterile solution of Cyanocobalamin in Water for Injection containing sufficient Acetic Acid or Hydrochloric Acid to adjust the pH to about 4. It may also contain suitable buffering agent. It contains not less than 95.0 per cent and not more than 110.0 per cent of the stated amount of $C_{63}H_{88}CoN_{14}O_{14}P$.

Identification : Complies with **Identification** test (A) described under Cyanocobalamin.

pH : Between 3.8 and 5.5, Appendix 5.10.

Coloured impurities : Protect the solutions from light throughout the test. Extract a volume equivalent to 2 mg of anhydrous cyanocobalamin with three or more quantities, each of 1 ml, of a mixture of equal parts of *phenol* and *chloroform* until the aqueous layer is no longer red. To the combined extracts add 15 ml of *acetone* and 80 ml of *solvent ether*, mix, centrifuge, and decant the colourless, supernatant liquid. Wash the residue with successive, 50 ml quantities of *solvent ether* until no odour of *phenol* remains after the residual ether has been allowed to evaporate from the residue. Dissolve the residue in the minimum quantity of *water* and carry out the test for **Coloured impurities** described under Hydroxocobalamin.

Other requirements : Complies with the requirements stated under Injections.

Assay : Protect the solution from light throughout the assay.

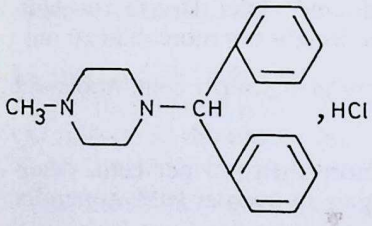
Measure the *extinction* at the maximum at about 361 nm of a 1-cm layer of solution containing not more than 25 µg of cyanocobalamin per ml, Appendix 5.15 A. Calculate the content of $C_{63}H_{88}CoN_{14}O_{14}P$, taking 207 as the value of E(1 per cent, 1-cm) at the maximum at about 361 nm.

CAUTION—In carrying out the **Identification** *test and the* **Assay**, *account must be taken of any added antimicrobial preservative.*

Storage : Store in single-dose or multiple-dose light-resistant containers.

Labelling : The label on the container states the strength in terms of the equivalent amount of anhydrous cyanocobalamin in a suitable dose-volume.

Cyclizine Hydrochloride



$C_{18}H_{22}N_2, HCl$ Mol. Wt. 302.85

Category : Antihistamine.

Dose : 25 to 50 mg.

Description : White, crystalline powder; almost odourless; taste, bitter.

Solubility : Slightly soluble in *water* and in *alcohol*, sparingly soluble in *chloroform*, practically insoluble in *solvent ether*.

Standards : Cyclizine Hydrochloride is the hydrochloride of 1 benzhydryl-4-methylpiperazine. It contains not less than 98.0 per cent and not more than the equivalent of 100.5 per cent of $C_{18}H_{22}N_2$,HCl calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *cyclizine hydrochloride R.S.*, Appendix 5.15 B.

(B) Dissolve 0.5 g in 10 ml of *alcohol (60 per cent)* warming if necessary, cool in ice, add 1 ml of *sodium hydroxide solution* and 20 ml of *water*, stir well, and filter; the precipitate obtained after washing with *water* and drying "in vacuo at 60°" for two hours, melts at about 108°, Appendix 5.11.

(C) It melts at about 285°, with decomposition, Appendix 5.11.

pH : Between 4.5 and 5.5, determined in a 2 per cent w/v solution in *alcohol (40 per cent)*, Appendix 5.10.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

N-Methylpiperazine : Complies with the test described under Chlorcyclizine Hydrochloride.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

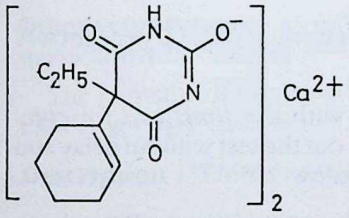
Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 130°, Appendix 5.8.

Assay : Weigh accurately about 0.4 g, dissolve in 80 ml of *glacial acetic acid*, and 10 ml of *mercuric acetate solution* and titrate with *0.1N perchloric acid*, determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.01514 g of $C_{18}H_{22}N_2$, HCl.

Storage : Store in well-closed, light-resistant containers.

Cyclobarbitone Calcium

Cyclobarbital Calcium



$C_{24}H_{30}CaN_4O_6$ Mol. Wt. 510.67

Category : Hypnotic; sedative.

Dose : 200 to 400 mg.

Description : White or slightly yellowish crystalline powder, odourless; taste, bitter and persistent.

Solubility : Slightly soluble in *water*; very slightly soluble in *alcohol*; practically insoluble in *chloroform* and in *solvent ether*.

Standards : Cyclobarbitone Calcium is calcium 5-(cyclohex-1-enyl)-5-ethylbarbiturate. It contains not less than 98.5 per cent and not more than the equivalent of 102.0 per cent of $C_{24}H_{30}CaN_4O_6$, calculated with reference to the dried substance.

Identification : (A) Dissolve 0.4 g with heating in a mixture of 10 ml of *water* and 10 ml of *5N acetic acid*, cool, filter, wash the precipitate with three quantities, each of 2 ml, of *water* and dry at about 105°; the dried precipitate melts at about 172°, Appendix 5.11, and gives the reactions of *barbiturates*, Appendix 3.1.

(B) Dissolve 10 mg of the precipitate obtained in **Identification** test A in 1 ml of *sulphuric acid*; a yellowish colour is produced which turns orange after a few minutes.

(C) The filtrate obtained in **Identification** test A gives the reactions of *calcium*, Appendix 3.1.

Oxidation products : To 1.0 g add 2.5 ml of *2N sodium hydroxide* and 2.5 ml of *water*; the mixture does not become coloured within two minutes.

Neutral and Basic substances : Complies with the test for **Neutral and basic substances** described under Amylobarbitone. The residue weighs not more than 3.0 mg.

Free cyclobarbitone : Shake 1.0 g successively with 50, 25 and 15 ml of *benzene*, filter and evaporate the solvent. The residue, after drying at 105° weighs not more than 30 mg.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105° for two hours, Appendix 5.8.

Assay : Weigh accurately about 0.25 g, add 5 ml of *pyridine* and 10 ml of *silver nitrate solution* in *pyridine*. Heat on a water-bath at 80° for five minutes until a clear solution is obtained. Cool, and titrate with *0.1N alcoholic sodium hydroxide*, using 0.25 ml of *thymolphthalein solution* as indicator, until a full blue colour is obtained. Each ml of *0.1N alcoholic sodium hydroxide* is equivalent to 0.02553 g of $C_{24}H_{30}CaN_4O_6$.

Storage : Store in well-closed, light-resistant containers.

Cyclobarbitone Tablets

Cyclobarbitone Calcium Tablets; Cyclobarbital Calcium Tablets

Category : Hypnotic; sedative.

Dose : Cyclobarbitone Calcium, 200 to 400 mg; not more than 1.2 g in twenty four hours.

Usual strength : 200 mg.

Standards : Cyclobarbitone Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Cyclobarbitone Calcium, $C_{24}H_{30}CaN_4O_6$.

Identification : (A) Triturate a quantity of the powdered tablets equivalent to about 0.5 g of Cyclobarbitone Calcium, with 25 ml of *water*, add 5 ml of *dilute hydrochloric acid*, boil, cool and extract with 20 ml of *solvent ether*, reserving the aqueous layer. Wash the ether extract with 10 ml of *water* and evaporate to dryness on a water-bath. Heat 0.2 g of the residue with 15 ml of *alcohol (25 per cent)* on a water-bath, filter while hot,

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

cool, and scratch the tube with a glass rod to induce crystallisation. The crystals, after washing with a small quantity of *alcohol (25 per cent)* and drying at 105°, melt at about 171°, Appendix 5.11, and give the reactions of *barbiturates*, Appendix 3.1.

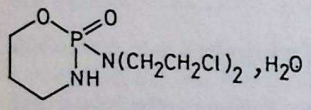
(B) The aqueous solution reserved in **Identification** test A gives the reactions of *calcium*, Appendix 3.1.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 0.5 g of Cyclobarbitone Calcium, add 10 ml of *N sodium hydroxide* and 40 ml of *water*, shake continuously for thirty minutes, and dilute to 100.0 ml with *water*. Filter, transfer 25.0 ml of the solution to a glass-stoppered flask, add 30.0 ml of *0.1N bromine* and 10 ml of *hydrochloric acid*, and allow to stand in ice for fifteen minutes shaking occasionally. Add 10 ml of *potassium iodide solution*, allow to stand in ice for further ten minutes and titrate the liberated iodine with *0.1N sodium thiosulphate*, using *starch solution*, added towards the end of the titration, as indicator. Perform a blank titration and make any necessary correction. Each ml of *0.1N bromine* is equivalent to 0.01277 g of $C_{24}H_{30}CaN_4O_6$.

Storage : Store in tightly-closed, light-resistant containers.

Cyclophosphamide



$C_7H_{15}Cl_2N_2O_2P, H_2O$ Mol. Wt. 279.10

Category : Antineoplastic; immunosuppressive.

Dose : By intravenous injection, 100 to 150 mg daily.

Description : Fine, white, crystalline powder; odourless or almost odourless; taste, slightly bitter. It liquefies upon loss of its water of crystallisation.

Solubility : Soluble in *water*; freely soluble in *alcohol*; slightly soluble in *solvent ether*.

Standards : Cyclophosphamide is the monohydrate of 2-bis(2-chloro-ethyl) aminoperhydro-1, 3, 2-oxazaphosphorinane 2-oxide. It contains not less than 98.0 per cent of $C_7H_{15}Cl_2N_2O_2P$, calculated with reference to the anhydrous substance.

Identification : (A) The *infra-red absorption spectrum* of a 5 per cent w/v solution in *chloroform* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of a similar solution of *cyclophosphamide R.S.*, Appendix 5.15 B.

(B) Dissolve 0.1 g in 10 ml of *water* and add 5 ml of *silver nitrate solution*; no precipitate is produced. Boil, a white precipitate is produced which is insoluble in *nitric acid* but is soluble in *dilute ammonia solution* from which it can be re-precipitated by the addition of *nitric acid*.

(C) Dissolve 0.1 g in 3 ml of *nitric acid* and 1 ml of *sulphuric acid*, heat till brown fumes are evolved and the solution becomes colourless; cool, add 10 ml of *water* and heat again up to 60°; add 10 ml of *ammonium molybdate solution*; a bright colour develops and a yellow precipitate is slowly formed.

(D) To 0.1 g add 2 ml of *water* and 2 ml of *sulphuric acid* and boil; the solution becomes turbid. After cooling, carefully add 25 ml of 20 per cent w/v solution of *sodium hydroxide* and heat again. A moistened *red litmus paper* placed over the vapours turns blue.

Melting range : Between 49.5° and 53.0°, Appendix 5.11.

pH : Between 4.0 and 6.0, determined in 2.0 per cent w/v solution, Appendix 5.10.

Chloride : 1.0 g complies with the *limit test for chlorides*, Appendix 3.2.2; carry out the test without delay and maintain the temperature below 20°

Heavy metals : Not more than 20 parts per million determined by Method A on 1.0 g dissolved in 2 ml of *dilute acetic acid Sp.* and diluted to 25 ml with *water* and filtered if necessary, Appendix 3.2.4.

Water : Between 5.8 and 7.0 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately about 0.2 g into a long-necked flask and heat with 2 ml of *sulphuric acid* and 2.5 ml of *nitric acid* until brown fumes cease to be evolved. Cool, add 1 ml of *nitric acid* and heat again. Continue adding *nitric acid* and heating until brown fumes are no longer evolved and the solution is colourless when cold. Heat until dense, white fumes are evolved, cool, transfer the solution to a flask with the aid of 150 ml of *water*, add 50 ml of *citric-molybdic acid solution* and heat slowly to boiling-point. Swirling the flask continuously, add 25 ml of *quinoline solution* at first dropwise and then in a steady stream, heat on a water-bath for five minutes, and cool. Filter, wash the precipitate with *water* until free from acid, transfer the precipitate to flask with the aid of 100 ml of *water*, add 50 ml of *0.5N sodium hydroxide* and shake until dissolved. Titrate the excess of sodium hydroxide with *0.5N hydrochloric acid*, using *phenolphthalein-thymol blue solution* as indicator. Each ml of *0.5N sodium hydroxide* is equivalent to 0.005021 g of $C_7H_{15}Cl_2N_2O_2P$.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Cyclophosphamide Injection

Category : Antineoplastic; immunosuppressive.

Dose : Cyclophosphamide. By intravenous injection, 100 to 150 mg daily.

Standards : Cyclophosphamide Injection is a sterile solution of Cyclophosphamide in Water for Injection containing Sodium Chloride. It is prepared by dissolving the contents of a sealed container in the requisite amount of Water for Injection immediately before use. The sealed container contains a mixture of one hundred parts by weight of Cyclophosphamide and forty-five parts by weight of Sodium Chloride.

Uniformity of weight : Complies with the requirements for **Uniformity of weight**, described under Injections.

Content of active ingredients : Not less than 92.5 per cent and not more than 107.5 per cent of the stated amounts of Cyclophosphamide, $C_7H_{15}Cl_2N_2O_2, H_2O$ and Sodium Chloride, NaCl.

Other requirements : Complies with the requirements stated under Injections.

The contents of the sealed container comply with the following requirements :

Description : White crystalline powder.

Identification : (A) Extract a quantity equivalent to 0.2 g Cyclophosphamide with *solvent ether* and evaporate the extract to dryness. The residue complies with **Identification** tests (A) and (B) described under Cyclophosphamide.

(B) A solution (1 in 20) gives the reactions of *sodium*, and *chlorides*, Appendix 3.1.

pH : Between 4.0 and 6.0, determined in a 2.0 per cent w/v solution, Appendix 5.10.

Water : Between 4.0 and 5.0 per cent w/w, Appendix 3.3.25.

Assay : Dissolve the contents of ten containers in sufficient *water* to produce 200.0 ml.

For $C_7H_{15}Cl_2N_2O_2P, H_2O$— Place an accurately measured volume of the solution equivalent to about 0.2 g of Cyclophosphamide in a long-necked flask, carefully evaporate to low bulk, cool, add 2 ml of *sulphuric acid* and 2.5 ml of *nitric acid*, heat until brown fumes cease to be evolved, and complete the **Assay** described under Cyclophosphamide, beginning at the words "cool, add 1 ml of *nitric acid*...". Each ml of *0.5N sodium hydroxide* is equivalent to 0.005367 g of $C_7H_{15}Cl_2N_2O_2P,H_2O$.

For NaCl— Carry out the **Assay** described under Ammonium Chloride, using an accurately measured volume of the solution equivalent to about 0.2 g of sodium chloride diluted, if necessary, to about 35 ml with *water*, beginning at the words "add 3 ml of *nitric acid*...." and maintaining the temperature below 20° throughout the operations. Each ml of *0.1N silver nitrate* is equivalent to 0.005844 g of NaCl.

Storage : It should be used immediately after preparation as it deteriorates on storage.

Labelling : The label on the sealed container states (1) "Cyclophosphamide for Injection"; (2) the weight of Cyclophosphamide and Sodium Chloride contained in it; (3) the volume of Water for Injection to be added.

Cyclophosphamide Tablets

Category : Antineoplastic; immunosuppressive.

Dose : Cyclophosphamide, 100 to 150 mg daily.

Usual strengths : 25 mg; 50 mg.

Standards : Cyclophosphamide Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Cyclophosphamide, $C_7H_{15}Cl_2N_2O_2P, H_2O$. The tablets may be coated.

Identification : Extract a quantity of the powdered tablets equivalent to 0.25 g of Cyclophosphamide with *solvent ether* and evaporate the extract to dryness. The residue complies with **Identification** tests (A) and (B) described under Cyclophosphamide.

Acidity : Shake a quantity of the powdered tablets equivalent to 0.25 g of Cyclophosphamide with 20 ml of *carbon dioxide-free water*, filter and titrate the filtrate with *0.1N sodium hydroxide* using *phenolphthalein solution* as indicator; not more than 0.2 ml of *0.1N sodium hydroxide* is required.

Other requirements : Comply with the requirements stated under Tablets.

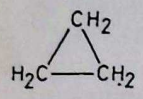
Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powdered tablets equivalent to about 0.2 g of Cyclophosphamide and extract with four quantities, each of 10 ml, of *solvent ether*, filtering the extracts through a plug of cotton wool and washing the plug with a further 10 ml of *solvent ether*. Transfer the combined etheral solutions to a long-necked flask, remove the ether, add 2 ml of *sulphuric acid* and 2.5 ml of *nitric acid* and heat until brown fumes cease to be evolved; cool and complete the **Assay** described under Cyclophosphamide, beginning at the words "add 1 ml of *nitric acid*.....". Each ml of *0.5N sodium hydroxide* is equivalent to 0.005367 g of $C_7H_{15}Cl_2N_2O_2P, H_2O$.

Storage : Store in tightly-closed containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Cyclopropane



C_3H_6 Mol. Wt. 42.08

Category : General anaesthetic.

Description : Colourless gas at atmospheric temperature and pressure; odour, characteristic. Flammable.

NOTE—Mixtures of cyclopropane with oxygen or air at certain concentrations are explosive.

Solubility : Very soluble in *alcohol*, in *solvent ether* and in *chloroform*. One volume, measured at normal temperature and pressure, dissolves in 2.85 volumes of *water*.

Standards : Cyclopropane contains not less than 99.0 per cent v/v of C_3H_6.

Acidity or Alkalinity : Dilute 0.3 ml of *methyl red solution* with 400 ml of boiling *water* and boil the solution for five minutes. Cool to about 80° and pour 100 ml of the solution into each of three matched *Nessler cylinders* marked A, B and C. To cylinder B add 0.2 ml of *0.01N hydrochloric acid* and to cylinder C add 0.4 ml of *0.01N hydrochloric acid*. Stopper both cylinders and cool to room temperature. Pass a volume of gas equivalent to 2000 ml, measured at normal temperature and pressure, through the solution in cylinder B, the time occupied being about thirty minutes. The colour of the solution in cylinder B is not deeper red than that of the solution in cylinder C and not deeper yellow than that of the solution in cylinder A.

Carbon dioxide : Pass a volume of gas equivalent to 1000 ml at normal temperature and pressure at a rate not exceeding 4000 ml per hour through 100 ml of a 3 per cent w/v solution of *barium hydroxide* contained in a vessel such that the depth of the solution is between 12 and 14 cm, using a delivery tube having a bore of about 1 mm and extending to within 2 mm of the bottom of the vessel; the turbidity produced is not greater than that produced by adding 1 ml of a solution of 0.1 g of *sodium bicarbonate* in 100 ml of *carbon dioxide-free water* to 100 ml of 3 per cent w/v solution of *barium hydroxide*.

Ethyl alcohol and water; Unsaturated substances : Pass a volume of gas equivalent to 1000 ml, measured at normal temperature and pressure, through a weighed tube containing *potassium hydroxide* in small pieces, the time occupied being forty to sixty minutes; the increase in weight of the tube is not more than 0.0056 g equivalent to 0.3 per cent w/w of the Cyclopropane.

Pass the gas from the tube of potassium hydroxide through a gas washing trap provided with a sintered glass bubbler containing 20.0 ml of *iodine monochloride solution* and connected in series with two gas washing bottles containing, respectively, 5.0 ml of *iodine monochloride solution* and 10 ml of *potassium iodide solution*. Mix the contents of the trap and washing bottles and titrate with *0.1N sodium thiosulphate*. Add 10 ml of *potassium iodide solution* to 25.0 ml of *iodine monochloride solution* and titrate with *0.1N sodium thiosulphate*. The difference between the titrations does not exceed 1.8 ml, equivalent to 0.2 per cent w/w of unsaturated substances calculated as propylene.

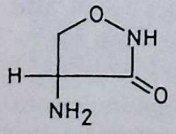
Halogen-containing substances : Pass a volume of gas equivalent to 1000 ml, measured at normal temperature and pressure, with the necessary amount of air into a small mixing chamber and pass the resulting mixture through a heated quartz tube containing pieces of platinised quartz, or through a heated silica tube containing sintered silica plates or pieces of platinised quartz, the time occupied being not less than forty minutes. Absorb the products of combustion in 50 ml of a 3 per cent w/v solution of *sodium peroxide*. Boil the solution for about ten minutes, cool, neutralise with a solution of *nitric acid* (containing about 30 per cent w/w of HNO_3) and add 5 ml of *2N nitric acid* to give the test solution. To 50 ml of the same solution of *sodium peroxide* which has been boiled, cooled, neutralised and acidified in the same manner, add 7.5 ml of *0.001N potassium bromide* to give the standard solution. Transfer the solutions to 100 ml matched *Nessler cylinders*, add 1.0 ml of *0.1N silver nitrate* to each, dilute to 100 ml with *water*, mix well, and allow to stand in the dark for fifteen minutes. Compare the turbidities of the two solutions; the turbidity of the test solution does not exceed that of the standard solution.

Assay : Place in a suitable nitrometer containing mercury, a volume of the material liquefied under pressure equivalent to 80 to 100 ml of the gas measured at normal temperature and pressure, add 25 ml of *sulphuric acid*, and allow to stand for fifteen minutes; not less than 99.0 per cent v/v is absorbed.

Storage : Store under pressure in metal cylinders in a cool place.

Labelling : The metal cylinder is painted orange and on the shoulder is stencilled the name of the gas or the symbol C_3H_6.

Cycloserine



$C_3H_6N_2O_2$ Mol.Wt. 102.09

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Category : Antibacterial (tuberculostatic).

Dose : 0.25 to 0.75 g daily, in divided doses.

Description : White or pale-yellow, crystalline powder; odourless or almost odourless; taste, slightly bitter; hygroscopic.

Solubility : Freely soluble in *water*; soluble in *alcohol*; slightly soluble in *chloroform*, and in *solvent ether*.

Standards : Cycloserine is (*R*)-4-aminoisoxazolidin-3-one, an antimicrobial substance produced by the growth of certain strains of *Streptomyces orchidaceus* or *S. qaryphalus*, or obtained by synthesis. It contains not less than 98.0 per cent of $C_3H_6N_2O_2$, calculated with reference to the dried substance.

Identification : (A) The light absorption in the range 215 to 350 nm of a 1-cm layer of a 0.00125 per cent w/v solution in *0.1N hydrochloric acid* exhibits a maximum only at 219 nm; *extinction* at 219 nm, about 0.43, Appendix 5.15 A; measure the *extinction* within fifteen minutes of preparing the solution.

(B) To 1 ml of a 0.01 per cent w/v solution in *0.1N sodium hydroxide*, add 3 ml of *dilute acetic acid* and 1 ml of a freshly prepared mixture of equal parts of a 4 per cent w/v solution of *sodium nitroprusside* and *sodium hydroxide solution*; a blue colour gradually develops.

(C) It melts at about 154°, Appendix 5.11.

Specific optical rotation : Between +110° and +114°, determined in a 5 per cent w/v solution in *2N sodium hydroxide*, Appendix 5.12.

Condensation products : *Extinction* of a 1-cm layer of a 0.04 per cent w/v solution in *0.1N sodium hydroxide* at the maximum at about 285 nm, not more than 0.32, Appendix 5.15 A.

pH : Between 5.5 to 6.5, determined in a 10 per cent w/v solution, Appendix 5.10.

Undue toxicity : Complies with the test described under Bacitracin, using 15 mg dissolved in 0.5 ml of *water for injection*.

Sulphated ash : Not more than 0.5 per cent, Appendix 3.2.7.

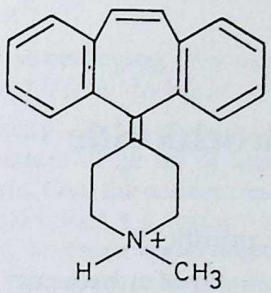
Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying "in vacuo at 60°" for three hours, Appendix 5.8.

Assay : Weigh accurately about 0.1 g and dissolve in 5 ml of *water*, add 75 ml of *isopropyl alcohol* and titrate with *0.1N sodium hydroxide (carbonate-free)* using *thymolphthalein solution* as indicator. Repeat the operation without the Cycloserine; the difference between the titrations represents the amount of sodium hydroxide required. Each ml of *0.1N sodium hydroxide* is equivalent to 0.010210 g of $C_3H_6N_2O_2$.

Storage : Store in well-closed containers in a cool place.

Labelling : The label on the container states (1) the date after which the contents are not intended to be used; (2) the storage conditions.

Cyproheptadine Hydrochloride



$C_{21}H_{21}N,HCl,1\frac{1}{2}H_2O$ Mol. Wt. 350.89

Category : Antihistaminic; antipruritic.

Dose : 4 to 20 mg daily, in divided doses.

Description : White or slightly yellow, crystalline powder; almost odourless; taste, slightly bitter.

Solubility : Slightly soluble in *water*, sparingly soluble in *alcohol*, soluble in *chloroform*; freely soluble in *methyl alcohol*, insoluble in *solvent ether*.

Standards : Cyproheptadine Hydrochloride is sesquihydrate or 4-(dibenzo [*a,d*] cyclohept-5-enylidene)-1-methylpiperidinium chloride. It contains not less than 98.5 per cent and not more than the equivalent of 101.0 per cent of $C_{21}H_{21}N$, HCl, calculated with reference to the dried substance.

Identification : (A) *The infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *cyproheptadine hydrochloride R.S.*, Appendix 5.15 B.

(B) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.0016 per cent w/v solution in *alcohol* exhibits a maximum only at 286 nm; *extinction* at 286 nm, about 0.5, Appendix 5.15 A.

(C) A saturated solution gives the reactions of *chlorides*, Appendix 3.1.

Heavy metals : Not more than 30 parts per million, determined on 0.66 g by Method B, Appendix 3.2.4.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Loss on drying : Not less than 7.0 per cent and not more than 9.0 per cent determined on 0.5 g by drying "in vacuo at 100°", Appendix 5.8.

Assay : Weigh accurately about 0.5 g and dissolve with aid of heat in 20 ml of *glacial acetic acid*. Add 10 ml *mercuric acetate solution* and 0.5 ml *acetic anhydride*. Titrate with *0.1N perchloric acid*, using *crystal-violet solution* as indicator, until the colour changes from purple to green-blue. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.03239 g of $C_{21}H_{21}N$,HCl.

Storage : Store in well-closed containers.

Cyproheptadine Hydrochloride Syrup

Category : Antihistaminic; antipruritic.

Dose : The equivalent of 4 to 20 mg of anhydrous cyproheptadine hydrochloride, daily, in divided doses.

Usual strength : 2 mg of anhydrous cyproheptadine hydrochloride in 5 ml.

Standards : Cyproheptadine Hydrochloride Syrup contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Cyproheptadine Hydrochloride, $C_{21}H_{21}N$, HCl.

Identification : To 5 ml add 5 ml of a 1.0 per cent w/v solution of *sodium bicarbonate* and extract with three quantities, each of 15 ml, of *iso-octane*. Wash the combined iso octane extracts with 5 ml of the sodium bicar bonate solution and discard the washings. Evaporate the iso-octane solution to dryness on a water-bath and dissolve the residue in 100 ml of *alcohol* The light absorption of the resulting solution, in the range 230 to 350 nm, exhibits a maximum only at 286 nm, Appendix 5.15 A.

pH : Between 3.5 and 4.5, Appendix 5.10.

Assay : To an accurately measured volume equivalent to 2 mg of anhydrous cyproheptadine hydrochloride add 20 ml of a 1.0 per cent w/v solution of *sodium bicarbonate* and extract with two quantities, each of 25 ml, of *iso-octane*. Wash the combined iso-octane extracts with 5 ml of the sodium carbonate solution and discard the washings. Extract the iso-octane solution with 50 ml of *0.1N sulphuric acid* and collect the aqueous extract in a 100-ml volumetric flask. Extract the iso-octane solution with 25 ml of *0.1N sulphuric acid* and combine the aqueous extracts in the volumetric flask. Dilute to volume with *0.1N sulphuric acid* and mix. Filter a portion of the solution through a dry filter paper and discard the first 20ml of the filtrate. Measure the *extinction* of a 1-cm layer of the filtrate at the maximum at about 286 nm, Appendix 5.15 A, using *0.1N sulphuric acid* as a blank. Calculate the content of $C_{21}H_{21}N$, HCl, taking 355 as the value of E(1 per cent, 1-cm) at the maximum at about 286 nm.

Storage : Store in light-resistant containers.

Cyproheptadine Tablets

Cyproheptadine Hydrochloride Tablets

Category : Antihistaminic; antipruritic.

Dose : The equivalent of 4 to 20 mg of anhydrous cyproheptadine hydrochloride, daily, in divided doses.

Usual strength : The equivalent of 4 mg anhydrous cyproheptadine hydrochloride.

Standards : Cyproheptadine Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Cyproheptadine Hydrochloride, $C_{21}H_{21}N$, HCl.

Identification : (A) The light absorption of the solution obtained in the **Assay**, in the range 230 to 350 nm exhibits a maximum only at 286 nm.

(B) Extract a quantity of the powdered tablets equivalent to 20 mg of anhydrous cyproheptadine hydrochloride with 7 ml of *water*, filter, add 0.3 ml of *dilute ammonia solution* to the filtrate, and again filter; the filtrate yields the reactions of *chlorides*, Appendix 3.1.

Uniformity of content : Powder one tablet, warm with 20 ml of *alcohol* and centrifuge. Repeat the extraction with three further quantities, each of 20 ml of *alcohol*. Cool the combined extracts and add sufficient *alcohol* to produce 200.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 286 nm, Appendix 5.15 A. Calculate the content of $C_{21}H_{21}N$, HCl, taking 355 as the value of E(1 per cent, 1-cm) at the maximum at about 286 nm.

Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 90 and 110 per cent of the average except that for one tablet the content may be between 85 and 115 per cent of the average.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of powder equivalent to 1.5 mg of anhydrous cyproheptadine hydrochloride, add sufficient *alcohol* to produce 100.0 ml and filter, if necessary. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 286 nm, Appendix 5.15 A. Calculate

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

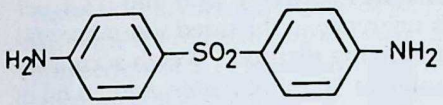
Digitized by Arya Samaj Foundation Chennai and eGangotri

the content of $C_{21}H_{21}N,HCl$, taking 355 as the value of E (1 per cent, 1-cm) at the maximum at about 286 nm.

Labelling : The label states the quantity of the active ingredient in terms of the equivalent amount of anhydrous cyproheptadine hydrochloride.

Dapsone

D.D.S.



$C_{12}H_{12}N_2O_2S$ Mol. Wt. 248.30

Category : Antibacterial (leprostatic).

Dose : Initial dose, 25 to 50 mg twice weekly, increasing by 50 to 100 mg every month, to a maximum of 200 to 400 mg twice weekly.

Description : White or creamy-white, crystalline powder; odourless; taste, slightly bitter.

Solubility : Very slightly soluble in *water*, freely soluble in *alcohol*, soluble in dilute mineral acids.

Standards : Dapsone is bis (4-aminophenyl) sulphone. It contains not less than 99.0 per cent and not more than the equivalent of 100.5 per cent of $C_{12}H_{12}N_2O_2S$, calculated with reference to the dried substance.

Identification : (A) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of 0.005 per cent w/v solution in *methyl alcohol* exhibits maxima at 260 nm and at 295 nm; *extinction* at 260 nm, about 0.365 and at 295 nm, about 0.6, Appendix 5.15 A.

(B) Dissolve 50 mg in 2 ml of warm *dilute hydrochloric acid*, cool in ice and add 2 ml of a 1 per cent w/v solution of *sodium nitrite*, add 2 ml of *water*, and 1 ml of a freshly prepared *β-naphthol solution* containing 0.5 g of *sodium acetate*; a scarlet precipitate is produced.

(C) Carry out the method described under **Related substances** applying separately to the plate 1 µl of each of two solutions in *methyl alcohol* containing (1) 0.1 per cent w/v of the substance being examined and (2) 0.1 per cent w/v of *dapsone R.S.* The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

Melting range : Between 176° and 181°, Appendix 5.11.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 8 volumes of *toluene* and 4 volumes of *acetone* as the mobile phase. Apply separately to the plate 10 µl of each of three solutions of the substance being examined, in *methyl alcohol* containing (1) 1.0 per cent w/v; (2) 0.01 per cent w/v and (3) 0.002 per cent w/v. After removal of the plate, allow it to dry in air and spray with a 0.5 per cent w/v solution of *sodium nitrite* in *0.1N hydrochloric acid* and while still damp, with a 0.1 per cent w/v solution of *N-(1-naphthyl) ethylenediamine hydrochloride*. Any spots in the chromatogram obtained with solution (1) other than the principal spot, are not more intense than the spots in the chromatogram obtained with solution (2) and not more than two of any such spots are more intense than the spots in the chromatogram obtained with solution (3).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.3 g and dissolve in a mixture of 20 ml of *water* and 20 ml of *hydrochloric acid*. Cool the solution and carry out the *nitrite titration*, Appendix 3.3.4. Perform a blank determination and make any necessary correction. Each ml of *0.1N sodium nitrite* is equivalent to 0.01242 g of $C_{12}H_{12}N_2O_2S$.

Storage : Store in well-closed containers.

Dapsone Tablets

D.D.S. Tablets

Category : Antibacterial (leprostatic).

Dose : Dapsone. Initial dose 25 to 50 mg twice weekly, increasing by 50 to 100 mg every month to a maximum of 200 to 400 mg twice weekly.

Usual strengths : 25 mg; 50 mg; 100 mg.

Standards : Dapsone Tablets contain not less than 93.0 per cent and not more than 107.0 per cent of the stated amount of Dapsone, $C_{12}H_{12}N_2O_2S$. The tablets may be coloured.

Identification : (A) Shake a quantity of the powdered tablets equivalent to 0.2 g of Dapsone with 15 ml of *dry acetone*, filter, and remove the solvent. The residue, when dried at 105°, melts at about 176°, Appendix 5.11, and complies with **Identification** tests (A) and (B) described under Dapsone.

(B) Carry out the method described under **Related substances**, applying separately to the plate 1 µl of each of the following two solutions: For solution (1) shake a quantity of the powdered tablets equivalent to 10 mg of Dapsone with 10 ml of *methyl alcohol* and shake; (2) a 0.1 per cent w/v solution of *dapsone R.S.* in *methyl alcohol*. The principal spot in the chromatogram

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

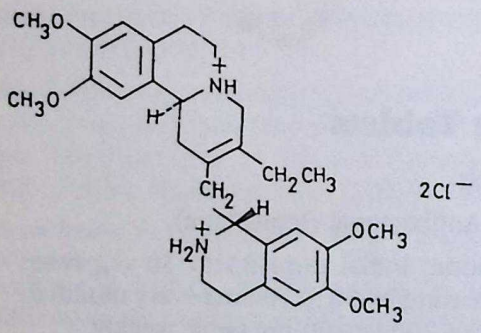
Related substances : Comply with the test for **Related substances** described under Dapsone, applying to the plate 10 µl of each of the following solutions: For solution (1) shake a quantity of the powdered tablets equivalent to 0.1 g of Dapsone with 10 ml of *methyl alcohol* and filter; for solution (2) dilute 1 volume of solution (1) to 100 volumes with *methyl alcohol*; for solution (3) dilute 1 volume of solution (2) to 5 volumes with *methyl alcohol*.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh 20 tablets and reduce to a *fine powder*. Carry out the **Assay** described under Dapsone, using an accurately weighed quantity of the powder equivalent to 0.25 g of Dapsone.

Storage : Store in well-closed containers.

Dehydroemetine Hydrochloride



$C_{29}H_{38}N_2O_4, 2HCl$ Mol.Wt. 551.55

Category : Anti-amoebic.

Dose : By deep subcutaneous or intramuscular injection, 60 to 90 mg daily.

Description : White to yellowish-white, crystalline powder; odourless; taste, bitter.

Solubility : Soluble in *water*; slightly soluble in *alcohol*.

Standards : Dehydroemetine Hydrochloride is the dihydrochloride of 2,3-didehydro-6′,7′,10,11-tetramethoxyemetan. It contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of $C_{29}H_{38}N_2O_4, 2HCl$, calculated with reference to the dried substance.-

Identification : (A) Add 2 mg to 1 ml of *sulphuric acid* containing about 5 mg of *molybdic acid*; a green colour develops.

(B) The light absorption in the range 230 to 350 nm, of a 1-cm layer of a 0.005 per cent w/v solution in *0.1N hydrochloric acid* exhibits a maximum only at 282 nm; *extinction* at 282 nm, about 0.62, Appendix 5.15 A.

(C) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

pH : Between 3.5 and 5.0, determined in a 3.0 per cent w/v solution, Appendix 5.10.

Heavy metals : Not more than 20 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

Hydrochloride content : Between 13.0 and 13.4 per cent, calculated with reference to the dried substance and determined by the following method : Weigh accurately about 0.4 g and dissolve in 50 ml of *water*. Add 10 ml of *dilute nitric acid* and titrate with *0.1N silver nitrate*, determining the end-point potentiometrically. Each ml of *0.1N silver nitrate* is equivalent to 0.003646 g of HCl.

Sulphated ash : Not more than 0.1 per cent , Appendix 3.2.7.

Loss on drying : Not more than 7.0 per cent, determined on 0.5 g by drying "in vacuo at 100°" for four hours, Appendix.5.8.

Assay : Weigh accurately about 0.4 g and dissolve in 40 ml of *glacial acetic acid*. Add 3 ml of *mercuric acetate solution*, 0.1 ml of *crystal-violet solution* and titrate with *0.1N perchloric acid* to a blue-green end-point. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02758 g of $C_{29}H_{38}N_2O_4, 2HCl$.

Storage : Store in well-closed, light-resistant containers.

Dehydroemetine Injection

Category : Anti-amoebic.

Dose : Dehydroemetine Hydrochloride. By deep subcutaneous or intramuscular injection, 60 to 90 mg daily.

Usual strength : 30 mg per ml.

Standards : Dehydroemetine Injection is a sterile solution of Dehydroemetine Hydrochloride in Water for Injection containing sufficient dilute hydrochloric acid to adjust the pH of the solution to 3.0. It contains not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of $C_{29}H_{38}N_2O_4, 2HCl$.

Description : Clear, almost colourless solution.

Identification : (A) To a volume equivalent to 30 mg of

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Dehydroemetine Hydrochloride add 1 ml of *0.1N iodine*. A yellowish-brown precipitate is produced.

(B) To a volume equivalent to 15 mg of Dehydroemetine Hydrochloride add 1 ml of *potassium mercuri-iodide solution*; a white precipitate is produced.

pH : Between 2.8 and 5.0, Appendix 5.10.

Other requirements : Complies with the requirements stated under Injection.

Assay : Measure accurately a volume equivalent to 60 mg of Dehydroemetine Hydrochloride and dilute to 100.0 ml with *0.1N hydrochloric acid*. Dilute 5.0 ml to 100.0 ml with *0.1N hydrochloric acid* and mix. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 282 nm, Appendix 5.15 A, using *0.1N hydrochloric acid* as a blank. Calculate the contents of $C_{29}H_{38}N_2O_4$, 2HCl, taking 123 as the value of E(1 per cent, 1-cm) at the maximum at about 282 nm.

Storage : Store in single-dose, light-resistant containers.

Dehydroemetine Tablets

Category : Anti-amoebic.

Dose : Dehydroemetine Hydrochloride, upto 60 mg, daily.

Usual strength : 10 mg.

Standards : Dehydroemetine Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Dehydroemetine Hydrochloride, $C_{29}H_{38}N_2O_4$, 2HCl. The tablets may be coated.

Identification : (A) Shake a quantity of the powdered tablets equivalent to 50 mg of Dehydroemetine Hydrochloride with 10 ml of *water* for a few minutes and filter; to 2 ml of the filtrate add 0.5 ml of *0.1N iodine*. A yellowish-brown precipitate is produced.

(B) To another 2 ml of the filtrate obtained in **Identification** test (A) add 1 ml of *potassium mercuri-iodide solution*; a white precipitate is produced.

Uniformity of content : Powder one tablet, warm with 20 ml of *0.1N hydrochloric acid* and centrifuge. Repeat the extraction with three further quantities, each of 20 ml, of *0.1N hydrochloric acid*. Cool the combined extracts and add sufficient *0.1N hydrochloric acid* to produce 200.0 ml. Dilute 25.0 ml to 50.0 ml with *0.1N hydrochloric acid* and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 282 nm, Appendix 5.15 A, using *0.1N hydrochloric acid* as the blank. Calculate the content of $C_{29}H_{38}N_2O_4$, 2HCl, taking 123 as the value of E(1 per cent, 1-cm) at the maximum at about 282 nm.

Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 90 and 110 per cent of the average except that for one tablet the content may be between 85 and 115 per cent of the average.

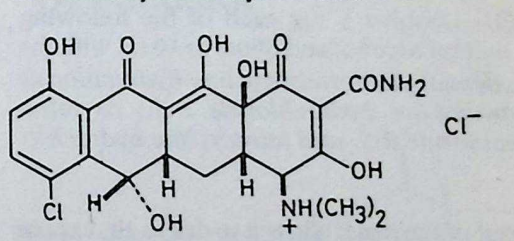
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 60 mg of Dehydroemetine Hydrochloride, shake with 40 ml of *0.1N hydrochloric acid*, heat gently, and centrifuge. Repeat the extraction with three further quantities, each of 20 ml, of *0.1N hydrochloric acid*. To the combined extracts add sufficient *0.1N hydrochloric acid* to produce 200.0 ml. Dilute 10.0 ml to 100.0 ml with *0.1N hydrochloric acid* and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 282 nm, Appendix 5.15 A, using *0.1N hydrochloric acid* as the blank. Calculate the content of $C_{29}H_{38}N_2O_4$, 2HCl, taking 123 as the value of E(1 per cent, 1-cm) at the maximum at about 282 nm.

Storage : Store in tightly-closed, light-resistant containers.

Demethylchlortetracycline Hydrochloride

Demeclocycline Hydrochloride



$C_{21}H_{21}ClN_2O_8$, HCl Mol. Wt. 501.32

Category : Antibacterial.

Dose : 0.6 to 1.8 g daily, in divided doses.

Description : Yellow crystalline powder; odourless; taste, bitter.

Solubility : Sparingly soluble in *water* and in *alcohol*; freely soluble in solutions of alkali hydroxides and carbonates; very slightly soluble in *chloroform* and in *solvent ether*.

Standards : Demethylchlortetracycline Hydrochloride is (4*S*, 4a*S*, 5a*S*, 6*S*, 12a*S*)-*N*-(2-carbamoyl-

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

7-chloro-1, 4, 4a, 5, 5a, 6, 11, 12a-octahydro-3, 6, 10, 12, 12a-pentahydroxy-1, 11-dioxonaphthacen-4-yl)-*N*, *N*-dimethylammonium chloride, an antimicrobial substance produced by the growth of certain strains of *Streptomyces aureofaciens* or by any other means. It contains not less than 900 µg per mg of $C_{21}H_{21}ClN_2O_8$, HCl, calculated with reference to the anhydrous substances.

Identification : (A) To 0.5 mg add 2 ml of *sulphuric acid*; a purple colour is produced. Add 1 ml of *water*; the colour is changed to yellow.

(B) To 2 mg add 5 ml of *hydrochloric acid* and boil for two minutes. A yellow colour is produced.

(C) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using as the coating substance a slurry prepared from 25 g of *kieselguhr G* and 50 ml of a mixture of 2.5 ml of *glycerin* and 47.5 ml of *0.1M disodium ethylenediaminetetraacetate* previously adjusted to pH 7.0 with *dilute ammonia solution*. Use a mixture of 40 volumes of *chloroform*, 40 volumes of *ethyl acetate* and 20 volumes of *acetone* as the mobile phase, the mixture being saturated with *0.1M disodium ethylenediaminetetraacetate*, previously adjusted to pH 7.0 with *dilute ammonia solution*. Apply separately to the plate, 1 µl of each of the solutions (1), (2) and (3) prepared as under :

Solution (1)—Dissolve 5 mg of the substance to be examined in *methyl alcohol* and dilute to 10 ml with the same solvent.

Solution (2)—Dissolve 5 mg of *demethylchlortetracycline hydrochloride R.S.* in *methyl alcohol* and dilute to 10 ml with the same solvent.

Solution (3)—Dissolve 5 mg each of the following substances in *methyl alcohol* and dilute to 10 ml with the same solvent; *demethylchlortetracycline hydrochloride R.S.*; *chlortetracycline hydrochloride R.S.*; *oxytetracycline hydrochloride R.S. and tetracycline hydrochloride R.S.*

After removal of the plate, allow it to dry in air, expose to the vapours of *strong ammonia solution* and examine under an ultra-violet lamp having a maximum output at about 366 nm. The separation is not valid unless the chromatogram obtained with solution (3) shows four spots. The principal spot in the chromatogram obtained with the solution (1) is similar in fluorescence, size and position to that in the chromatogram obtained with solution (2).

Light absorption : To 1 ml of a 0.01 per cent w/v solution in *0.001N hydrochloric acid* add 75 ml of *water* and 5 ml of *sodium hydroxide solution*; adjust the volume to 100 ml with *water*, mix immediately and measure the *extinction* of a 1-cm layer at 385 nm exactly five minutes after the addition of the *sodium hydroxide solution*; the *extinction* is not less than 0.342 and not more than 0.372, Appendix 5.15 A.

pH : Between 2.0 and 3.0, determined in a 1.0 per cent w/v solution, Appendix 5.10.

Sulphated ash : Not more than 0.5 per cent, Appendix 3.2.7.

Water : Not more than 2.0 per cent w/w, Appendix 3.2.25.

Assay : Carry out the *microbiological assay of antibiotics, Method B*, Appendix 4.1, and express the result in µg of demethylchlortetracycline hydrochloride per mg.

Storage : Store in tightly-closed, light-resistant containers.

Labelling : The label on the container states (1) the date after which the contents are not intended to be used; (2) the storage conditions.

Demethylchlortetracycline Capsules

Demeclocycline Capsules

Category : Antibacterial.

Dose : Demethylchlortetracycline Hydrochloride 0.6 to 1.8 g daily, in divided doses.

Usual strengths : 150 mg; 300 mg.

Standards : Demethylchlortetracycline Capsules contain not less than 90.0 per cent and not more than 120.0 per cent of the stated amount of Demethylchlortetracycline Hydrochloride $C_{21}H_{21}ClN_2O_8$, HCl.

Identification : To a quantity of the contents of the capsules equivalent to about 10 mg of Demethylchlortetracycline Hydrochloride, add 20 ml of warm *methyl alcohol*, allow to stand for twenty minutes, filter, and evaporate the filtrate to dryness on a water-bath. The residue complies with **Identification** tests (A), (B) and (C) described under Demethylchlortetracycline Hydrochloride.

Loss on drying : Not more than 5.0 per cent, determined on the contents of the capsules by drying 1.0 g "in vacuo at 60°" for three hours, Appendix 5.8.

Other requirements : Comply with the requirements stated under Capsules.

Assay : Weigh accurately a quantity of the mixed contents of 20 capsules equivalent to about 0.25 g of Demethylchlortetracycline Hydrochloride, add 500.0 ml of *0.1N hydrochloric acid*, mix, and carry out the

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

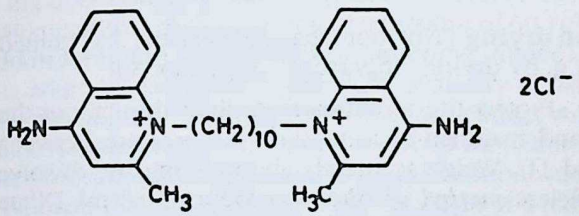
Digitized by Arya Samaj Foundation Chennai and eGangotri

microbiological assay of antibiotics, Method B, Appendix 4.1. Calculate the content of Demethylchlortetracycline Hydrochloride in the average weight of the content of the capsules.

Storage : Store in tightly-closed, light-resistant containers.

Labelling : The label on the container states (1) the date after which the capsules are not intended to be used; (2) the storage conditions.

Dequalinium Chloride



$C_{30}H_{40}Cl_2N_4$ Mol. Wt. 527.58

Category : Antiseptic.

Description : Creamy-white powder; odourless, taste, bitter.

Solubility : Slightly soluble in *water* and in *propylene glycol*; soluble in boiling *water*.

Standards : Dequalinium Chloride is 4, 4′- diamino-2, 2 -dimethyl-*N*, *N* -decamethylenedi(quinolinium chloride). It contains not less than 95.0 per cent and not more than the equivalent of 101.0 per cent of $C_{30}H_{40}Cl_2N_4$, calculated with reference to the dried substance.

Identification : (A) It melts at about 315° with decomposition, Appendix 5.11.

(B) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

(C) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.0008 per cent w/v solution exhibits three maxima, at 240 nm, 326 nm and 335 nm; *extinction* at 240 nm, about 0.65, at 326 nm, about 0.38 and at 335 nm, about 0.33, Appendix 5.15 A.

Acidity or Alkalinity : Shake 0.10 g for ten minutes with 100 ml of *carbon dioxide-free water*. Titrate with *0.1N hydrochloric acid* or *0.1N sodium hydroxide*, using *bromocresol purple solution* as indicator. Not more than 0.2 ml is required.

Non-quaternary amines : Not more than 1.0 per cent calculated as 4-aminoquinaldine, $C_{10}H_{10}N_2$, determined by the following method: Shake 1 g with 45 ml of *water* for five minutes, add 5 ml of *dilute nitric acid*, and shake for ten minutes. Filter through cotton wool. Transfer 20 ml of the filtrate to a separator, add 20 ml of *N sodium hydroxide*, extract with two quantities, each of 50 ml, of *solvent ether*, washing each extract in turn with the same 5 ml of *water*, and then extract each ether solution successively with 20 ml, 20 ml and 5 ml of *N hydrochloric acid*. Combine the acid extracts, dilute to 50 ml with *N hydrochloric acid*, and measure the *extinction* of a 1-cm layer of the resulting solution at 319 nm and 326.5 nm, Appendix 5.15 A. The ratio of the *extinction* at 319 nm to that at 326.5 nm is not less than 1.0. Calculate the content of $C_{10}H_{10}N_2$ from the expression 0.387a–0.306b, where a is E(1 per cent, 1-cm) at 319 nm and b is E (1 per cent, 1-cm) at 326.5 nm.

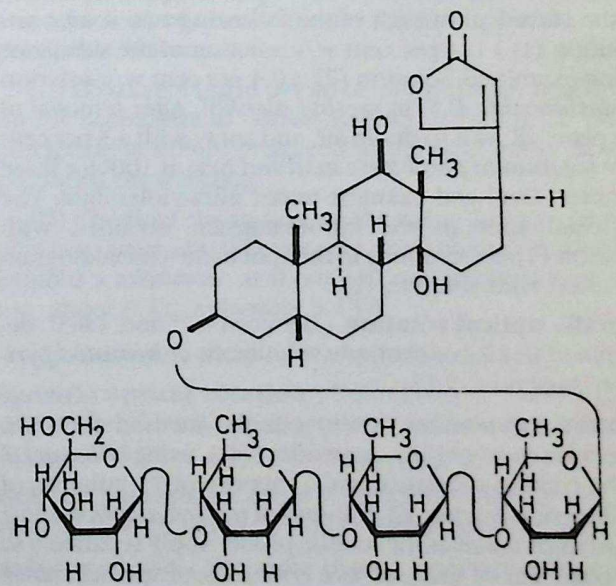
Loss on drying : Not more than 5.0 per cent, determined on 1.0 g by drying "in vacuo at 105°", for three hours, Appendix 5.8.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7

Assay : Weigh accurately about 0.7 g and dissolve in 80 ml of *glacial acetic acid* by warming gently under a reflux condenser, add 10 ml of *mercuric acetate solution* while hot, cool and titrate with *0.1N perchloric acid* in *dioxan* using 0.2 ml of *crystal-violet solution* as indicator, until the colour changes from violet-blue to pure blue. Carry out a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* in *dioxan* is equivalent to 0.02638 g of $C_{30}H_{40}Cl_2N_4$.

Storage : Store in well-closed containers.

Deslanoside



$C_{47}H_{74}O_{19}$ Mol. Wt. 943.09

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Category : Cardiotonic.

Dose : By intravenous or intramuscular injection, initial dose, 0.8 to 1.2 mg; maintenance dose, 0.4 mg at intervals of two to four hours.

Description : White crystals, or white crystalline powder; odourless; hygroscopic.

Solubility : Very slightly soluble in *water* and in *chloroform*; slightly soluble in *alcohol* and in *methyl alcohol*.

Standards: Deslanoside is 3-[{O-β-D-glucopyranosyl (1→4)-O-2,6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-O-2,6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-O-2,6-dideoxy-β-D-*ribo*-hexopyranosyl}oxy]-12, 14-dihydroxy-3β, 5β, 12β-card-20(22)-enolide. It contains not less than 95.0 per cent and not more than the equivalent of 104.0 per cent of $C_{47}H_{74}O_{19}$, calculated with reference to the dried substance.

Identification : (A) Dissolve 5 mg in 5 ml of *glacial acetic acid*, add 0.1 ml of *ferric chloride test-solution*, mix, and add 2 ml of *sulphuric acid* so as to form a subject layer; a brown ring is formed at the junction of the liquids and the upper layer develops a green colour which becomes blue on standing.

(B) Suspend 0.5 mg in 0.5 ml of *alcohol (60 per cent)* and add 0.25 ml of *dinitrobenzoic acid solution* and 0.1 ml of *dilute sodium hydroxide solution*; the suspension becomes violet.

(C) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 7 volumes of *benzene* and 3 volumes of *alcohol* as the mobile phase. Apply separately to the plate 5 µl of each of the following two solutions : Solution (1) a 0.4 per cent w/v solution of the substance being examined; solution (2) a 0.4 per cent w/v solution of *deslanoside R.S.* in *methyl alcohol*. After removal of the plate, allow it to dry in air, and spray with a 5 per cent w/v solution of *perchloric acid* and heat at 100° for three minutes. Cool and examine under ultra-violet light. The principal spot in the chromatogram obtained with solution (1) corresponds to the spot in the chromatogram obtained with solution (2).

Specific optical rotation : Between +7° and +8.5°, determined in a 2 per cent w/v solution in *dehydrated pyridine*, Appendix 5.12.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 75 volumes of *methylene chloride*, 23 volumes of *methyl alcohol*, and 2 volumes of *water* as the mobile phase. Apply separately to the plate 2µl of each of five solutions of the substance being examined in a mixture of equal volumes of *chloroform* and *methyl alcohol* containing (1) 1.0 per cent w/v, (2) 0.01 per cent w/v, (3) 0.02 per cent w/v, (4) 0.05 per cent w/v and (5) 0.1 per cent w/v. After removal of the plate allow it to dry in air, spray with a 10 per cent v/v solution of *sulphuric acid* in *alcohol* and heat at 140° for twenty minutes. Assess the combined intensities of any spots, other than the principal spot, in the chromatogram obtained with solution (1) by reference to the spots in the chromatograms obtained with solutions (2) and (4), making allowance for area in assessing the intensity of spots of different R_f values, and disregarding any spots less intense than the spot in the chromatogram obtained with solution (2). The combined intensity is less than the intensity of the spot in the chromatogram obtained with solution (5) and no spot is more intense than the spot in the chromatogram obtained with solution (4).

Sulphated ash : Not more than 0.2 per cent, Appendix 3.2.7.

Loss on drying : Not more than 8.0 per cent, determined on 0.5 g, by drying "in vacuo", Appendix 5.8.

Assay : Protect the solutions from light throughout the assay and maintain at a constant temperature between 19° and 21°. Weigh accurately about 30 mg and dissolve in sufficient *methyl alcohol* to produce 50.0 ml. Dilute 25.0 ml to 100.0 ml with *methyl alcohol*. To 10.0 ml of the resulting solution add 6 ml of *alkaline picric acid solution* and dilute to 25.0 ml with *water*. Allow to stand for 1 hour and measure the *extinction* of a 1-cm layer of the solution at the maximum at about 490 nm, using as a blank a mixture of 10 ml of *methyl alcohol* and 6 ml of *alkaline picric acid solution* diluted to 25 ml with *water*. Calculate the content of $C_{47}H_{74}O_{19}$ from the *extinction* obtained by simultaneously carrying out the operation using *deslanoside R.S.* instead of the substance being examined, and from the declared content of $C_{47}H_{74}O_{19}$ in the *deslanoside R.S.*

Storage : Store in tightly-closed, light-resistant containers.

Deslanoside Injection

Category : Cardiotonic.

Dose : Deslanoside, by intravenous or intramuscular injection; initial dose, 0.8 to 1.2 mg; maintenance dose, 0.4 mg at intervals of two to four hours.

Usual strength : 0.2 mg per ml.

Standards : Deslanoside Injection is a sterile solution of Deslanoside in Water for Injection containing suitable buffering agents. It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of $C_{47}H_{74}O_{19}$.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Identification : Complies with the **Identification** test (C) described under Deslanoside, using as solution (1) a solution prepared in the following manner : Transfer a volume of the Injection equivalent to about 2 mg of Deslanoside to a separator and extract with 25 ml of a mixture of 7 volumes of *chloroform* and 3 volumes of *alcohol*. Transfer the extract to a 10-ml flask and evaporate to dryness on a water-bath. Dissolve the residue in 0.5 ml of *methyl alcohol*.

pH : Between 5.9 and 6.5, Appendix 5.10

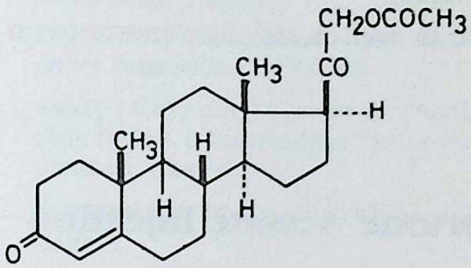
Other requirements : Complies with the requirements stated under Injections.

Assay : Protect the solutions from light throughout the assay and maintain at a constant temperature between 19° and 21°. To an accurately measured volume equivalent to 3 mg of Deslanoside, add 10 ml of *water* and extract with five quantities, each of 20 ml, of a mixture of 60 volumes *chloroform* and 40 volumes of *isopropyl alcohol*, with the addition of *sodium chloride* if necessary to disperse any emulsions that may form. Wash each extract with the same quantities of 20 ml and then of 10 ml *water*. Filter the combined extracts through a plug of cotton wool and evaporate the filtrate to dryness "in vacuo at a temperature of about 35°". Transfer the residue to a flask with *methyl alcohol* and add sufficient *methyl alcohol* to produce 20 ml. To 10 ml of the resulting solution add 6 ml of *alkaline picric acid solution* and dilute to 25 ml with *water*. Allow to stand for one hour and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 490 nm, Appendix 5.15 A, using as the blank a mixture of 10 ml of *methyl alcohol* and 6 ml of *alkaline picric acid solution* diluted to 25 ml with *water*. Calculate the content of $C_{47}H_{74}O_{19}$ from the *extinction* obtained by simultaneously carrying out the operation using a solution prepared by dissolving 30 mg of *deslanoside R.S.* in sufficient *methyl alcohol* to produce 50 ml, diluting 25 ml to 100 ml with *methyl alcohol* and continuing as described above, beginning at the words "To 10 ml of the resulting solution ....".

Storage : Store in single-dose, light-resistant containers.

Desoxycortone Acetate

Desoxycorticosterone Acetate; Deoxycortone Acetate



$C_{23}H_{32}O_4$ Mol. Wt. 372.50

Category : Adrenocortical steroid (salt-regulating).

Dose : By intramuscular injection, 2 to 5 mg daily.

Description : White or creamy-white crystalline powder; odourless.

Solubility : Practically insoluble in *water*; sparingly soluble in *alcohol*, and in *dioxan*.

Standards : Desoxycortone Acetate 21-hydroxy-4-pregnene-3,20-dione, 21-acetate. It contains not less than 96.0 per cent and not more than the equivalent of 104.0 per cent of $C_{23}H_{32}O_4$, calculated with reference to the dried substance.

Identification : (A) Complies with the test for *identification of steroids*, Appendix 3.3.11, using *solvent II* and *mobile phase E* and applying to the plate 2 µl of each of the solutions.

(B) Dissolve 40 mg in 1 ml of *methyl alcohol*, warm, and add 1 ml of *alkaline cupri-tartrate solution*; a red precipitate is formed.

(C) Dissolve 5 mg in 0.5 ml of *methyl alcohol*, add 0.5 ml of *ammoniacal silver nitrate solution*; a black precipitate is slowly produced in the cold but is rapidly produced on warming.

(D) The light absorption, in the range 220 to 350 nm, of a 1-cm layer of 0.001 per cent w/v solution in *alcohol* exhibits a maximum at about 240 nm; *extinction* at 240 nm, about 0.45, Appendix 5.15 A.

(E) It melts at about 158°, Appendix 5.11.

Specific optical rotation : Between +171° and +179°, determined in a 1.0 per cent w/v solution in *dioxan*, Appendix 5.12.

Related foreign steroids : Complies with the test for *related foreign steroids, Method B*, Appendix 3.3.12.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, deter-

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

mined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Carry out the **Assay** described under Betamethasone, using *desoxycortone acetate R.S.* for preparing the *standard solution.*

Storage : Store in well-closed, light-resistant containers.

Desoxycortone Acetate Injection

Desoxycorticosterone Acetate Injection

Category : Adrenocortical steroid (salt-regulating).

Dose : Desoxycortone Acetate. By intramuscular injection, 2 to 5 mg daily.

Usual strength : 5 mg per ml.

Standards : Desoxycortone Acetate Injection is a sterile solution of Desoxycortone Acetate in Ethyl Oleate or other suitable ester, in a suitable fixed oil, or in any mixture of these; it may contain suitable alcohols. It contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of $C_{23}H_{32}O_4$.

Identification : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 7 volumes of *heptane* and 3 volumes of *acetone* as the mobile phase. Apply separately to the plate 1 µl of each of two solutions prepared as follows. For solution (1) dilute the injection with *carbon tetrachloride*, to give a solution containing the equivalent of 0.25 per cent w/v Desoxycortone Acetate; solution (2) is a 0.25 per cent w/v solution of *desoxycortone acetate R.S.* in *carbon tetrachloride.* After removal of the plate, allow it to dry in air until the odour of the solvent is no longer detectable, spray with a 10 per cent w/v solution of *sulphuric acid* in *alcohol*, heat at 105° for thirty minutes, and examine under an ultraviolet lamp having a maximum output at about 366 nm. The spot in the chromatogram obtained with solution (1) corresponds with the spot in the chromatogram obtained with solution (2). Spots due to the vehicle also may be observed.

Other requirements : Complies with the requirement stated under Injections.

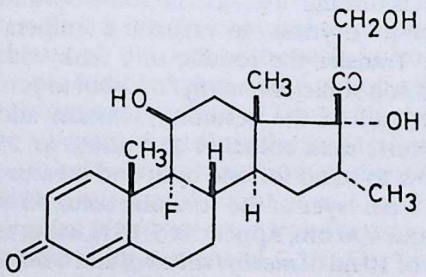
Assay : Add an accurately measured volume equivalent to 2.5 mg of Desoxycortone Acetate to 50 ml of *iso-octane* saturated with *alcohol*, mix, and extract with six quantities, each of 20 ml, of *alcohol*, saturated with *iso-octane.* Carefully evaporate the combined extracts just to dryness on a water-bath with the aid of a current of air. To the warm residue add 20 ml of *aldehyde-free ethyl alcohol*, stir to dissolve, transfer to a flask with the aid of further quantities of hot *aldehyde-free ethyl alcohol*, allow to cool and add sufficient *aldehyde-free ethyl alcohol* to produce 250.0 ml. On 20.0 ml of the resulting solution *(test-solution)* carry out the *assay of steroids*, Appendix 3.3.10, using *desoxycortone R.S.* to prepare the *standard solution.*

Storage : Store in single-dose or multiple-dose, light-resistant containers.

If solid matter separates on standing, it should be redissolved by warming before use.

Labelling : The label on the container states (1) the composition of the solvent; (2) "for intramuscular injection only"; (3) that any sediment should be dissolved by warming, before use.

Dexamethasone



$C_{22}H_{29}FO_5$ Mol. Wt. 392.47

Category : Adrenocortical steroid (anti-inflammatory).

Dose : 0.5 to 10 mg daily, in divided doses.

Description : White or almost white crystals or a crystalline powder; odourless.

Solubility : Practically insoluble in *water*; sparingly soluble in *alcohol*; very slightly soluble in *chloroform.*

Standards : Dexamethasone is 9α-fluoro-11β,17α,-21-trihydroxy-16α-methylpregna-1, 4-diene-3, 20-dione. It contains not less than 96.0 per cent and not more than the equivalent of 104.0 per cent of $C_{22}H_{29}FO_5$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths, and have similar relative intensities to, those in the spectrum of *dexamethasone R.S.*, Appendix 5.15 B.

(B) Place 2 ml of a 0.01 per cent w/v solution in *alcohol* in a stoppered tube, add 10 ml of *phenyl-*

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

hydrazine solution, mix and place in a water-bath at 60° for twenty minutes. Cool immediately and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 423 nm. The E(1 per cent, 1-cm) of the resulting solution at the maximum at about 423 nm is not less than 250, Appendix 5.15 A.

(C) Complies with the test for *identification of steroids*, Appendix 3.3.11, using *solvent I* and *mobile phase A*. At a fourth point apply 2 µl of a mixture of equal volumes of solution (1) and 0.25 per cent w/v solution of *betamethasone R.S.* The chromatogram obtained with this solution shows two closely-running spots.

Specific optical rotation : Between +72° and +80°, determined in a 1 per cent w/v solution in *dioxan*, Appendix 5.12.

Light absorption : *Extinction* of a 1-cm layer of a 0.001 per cent w/v solution in *methyl alcohol* at the maximum at about 240 nm, 0.38 to 0.41, Appendix 5.15 A; ratio of the *extinction* at the maximum at about 240 nm to that at 263 nm, 1.9 to 2.1.

Related foreign steroids : Complies with the test for *related foreign steroids, Method A*, Appendix 3.3.12.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying "in vacuo at 100°", Appendix 5.8.

Assay : Carry out the **Assay** described under Betamethasone, using *dexamethasone R.S.* for preparing the *standard solution*.

Storage : Store in well-closed light-resistant containers.

Dexamethasone Tablets

Category : Adrenocortical steroid (anti-inflammatory).

Dose : Dexamethasone, 0.5 to 10 mg daily, in divided doses.

Usual strength : 0.5 mg.

Standards : Dexamethasone Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Dexamethasone, $C_{22}H_{29}FO_5$.

Identification : Shake a quantity of the powdered tablets with *chloroform* and evaporate the extract to dryness; the residue complies with **Identification** tests (A) and (B) described under Dexamethasone.

Related foreign steroids : Carry out the test for **Related foreign steroids** described under Betamethasone Tablets, using a quantity of powdered tablets equivalent to 3 mg of Dexamethasone.

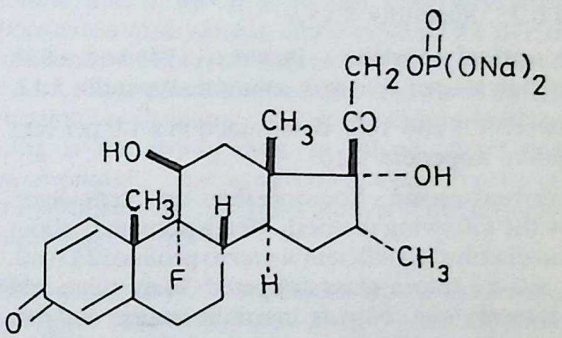
Other requirements : Comply with the requirements stated under Tablets.

Uniformity of content : Carry out the test described under Betamethasone Tablets.

Assay : Carry out the **Assay** described under Betamethasone Tablets, using *dexamethasone R.S.* for preparing the standard solution.

Storage : Store in well-closed, light-resistant containers.

Dexamethasone Sodium Phosphate



$C_{22}H_{28}FNa_2O_8P$ Mol. Wt. 516.41

Category : Adrenocortical steroid (anti-inflammatory).

Dose : By intravenous or intramuscular injection, the equivalent of 12 to 32 mg of dexamethasone phosphate, in the treatment of acute adrenal insufficiency.

4.4 mg of Dexamethasone Sodium Phosphate is approximately equivalent to 4 mg of dexamethasone phosphate.

Description : White or a slightly yellow crystalline powder; almost odourless; hygroscopic.

Solubility : Freely soluble in *water*; slightly soluble in *alcohol*; very slightly soluble in *dioxan*; practically insoluble in *chloroform* and in *solvent ether*.

Standards : Dexamethasone Sodium Phosphate is disodium 9α-fluoro-11β, 17α-dihydroxy-16α-methyl-3, 20-dioxopregna-1, 4-dien-21-yl-orthophosphate. It contains not less than 96.0 per cent and not more than the equivalent of 103.0 per cent of

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

$C_{22}H_{28}FNa_2O_8P$, calculated with reference to the anhydrous and alcohol-free substance.

Identification : (A) Dissolve about 5 mg in 2 ml of *sulphuric acid* and allow to stand for five minutes; a light yellowish-brown colour is produced. Dilute with 2 ml of *water*; an intense brownish-red colour is produced. Add 8 ml of *water*; a light yellowish-brown colour is again produced and a flocculent precipitate is formed.

(B) Complies with **Identification** test (C) described under Betamethasone Sodium Phosphate.

(C) Complies with **Identification** test (D) described under Betamethasone Sodium Phosphate, using as solution (2) a 0.25 per cent w/v of *dexamethasone sodium phosphate R.S.*

(D) To 2 ml of a 0.013 per cent w/v solution in *alcohol* in a stoppered tube add 10 ml of *phenylhydrazine solution*, mix, and place in a water-bath at 60° for twenty minutes. Cool immediately; *extinction* of a 1-cm layer of the resulting solution at the maximum at 423 nm, is not less than 0.25, Appendix 5.15 A.

Specific optical rotation : Between +74° and +82°, determined in a 1 per cent w/v solution, Appendix 5.12.

pH : Between 7.5 and 10.5, determined in a 1.0 per cent w/v solution, Appendix 5.10.

Free dexamethasone : Not more than 1 per cent, determined by the following method: Weigh accurately about 25 mg and dissolve in sufficient *water* to produce 25.0 ml. Transfer 5.0 ml into a glass-stoppered 50-ml tube, add 25.0 ml of *methylene chloride*, insert the stopper and mix by gentle shaking. Allow to stand until the methylene chloride layer is clear. Measure the *extinction* of a 1-cm layer of the resulting solution at about 236 nm, Appendix 5.15 A, using *methylene chloride* as the blank. Calculate the content of dexamethasone, taking 390 as the value of E(1 per cent, 1-cm) at about 236 nm.

Inorganic phosphates : Complies with the test for Inorganic phosphate described under Betamethasone Sodium Phosphate.

Alcohol : Not more than 8 per cent w/w, determined by the *gas-liquid chromatography method*, Appendix 5.4.1, using solutions in *water* containing (1) 1.0 per cent v/v of *n-propyl alcohol* (internal standard) and 1.0 per cent v/v of *ethyl alcohol*, (2) 10.0 per cent w/v of the substance being examined and (3) 10.0 per cent w/v of the substance being examined and 1.0 per cent v/v of the internal standard. Adjust the content of *ethyl alcohol* in solution (1) to produce a peak of similar height to the corresponding peak in the chromatogram obtained with solution (2). The chromatographic procedure may be carried out using (a) a column 1.5 m long and 4 mm in internal diameter packed with porous polymer beads (80 to 100 mesh) maintained at 135°, (b) nitrogen as the carrier gas, and (c) a flame ionisation detector Calculate the percentage w/w of alcohol, assuming the weight per ml at 25° to be 0.787 g.

Total alcohol and water : Not more than 16 per cent w/w, calculated by adding the percentage of alcohol and the percentage of *water*, determined on 0.3 g, Appendix 3.3.25.

Assay : Dissolve 0.2 g in sufficient *water* to produce 200.0 ml. Dilute 5.0 ml to 250.0 ml with *water* and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 241 nm, Appendix 5.15 A. Calculate the content of $C_{22}H_{28}FNa_2O_8P$, taking 297 as the value of E(1 per cent, 1-cm) at the maximum at about 241 nm.

Storage : Store in well-closed, light-resistant containers.

Dexamethasone Sodium Phosphate Injection

Category : Adrenocortical steroid (anti-inflammatory).

Dose : By intramuscular or by intravenous injection, the equivalent of 2 to 6 mg of Dexamethasone Phosphate per kg of body weight daily, in divided doses.

Usual strength : The equivalent of 4 mg of Dexamethasone Phosphate per ml. 4.4 mg of Dexamethasone Sodium Phosphate is approximately equivalent to 4 mg of Dexamethasone Phosphate.

Description : Clear, colourless solution.

Standards : Dexamethasone Sodium Phosphate Injection is a sterile solution of Dexamethasone Sodium Phosphate in Water for Injection. It contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Dexamethasone Phosphate, $C_{22}H_{30}FO_8P$.

Identification : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using a suitable silica gel as the coating substance and a mixture of 50 volumes of *chloroform*, 50 volumes of *acetone* and 1 volume of *water* as the mobile phase. Apply separately to the plate 5 µl of each of two solutions prepared as follows :

(1) Dilute a quantity of the injection equivalent to about 5 mg of Dexamethasone Phosphate with 25 ml of *water* and extract with two quantities, each of 25 ml, of *methylene chloride*. Discard the *methylene chloride* and transfer the aqueous layer to a 50-ml volumetric flask, dilute to volume with *water* and mix. Pipette 5 ml into a 50-ml glass-stoppered tube and incubate at 37° for forty-five minutes with 5 ml of *alkaline phosphate solution*. Extract with 25 ml of *methylene chloride*, evaporate

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

15 ml of the methylene chloride, extract to dryness and dissolve the residue in 1 ml of *methylene chloride*.

(2) Dissolve 30 mg of *dexamethasone R.S.* in sufficient *methylene chloride* to produce 100 ml. After removal of the plate allow it to dry in air until the odour of the solvent is no longer detectable, spray with a 50 per cent w/v solution of *sulphuric acid*, heat at 105° until brown or black spots appear. The main spot in the chromatogram obtained with solution (1) corresponds to that obtained with solution (2).

pH : Between 7.5 and 8.5, Appendix 5.10.

Other requirements : Complies with the requirements stated under Injections.

Assay : To an accurately measured volume equivalent to about 5 mg of Dexamethasone Phosphate, add 25 ml of *water* and extract with two quantities, each of 25 ml, of *methylene chloride* and discard the methylene chloride each time. Transfer the aqueous layer quantitatively to a 50-ml volumetric flask, dilute to volume with *water* and mix. Pipette 2.0 ml into a glass-stoppered tube, add 5.0 ml of a freshly prepared *phenylhydrazine solution*, stopper loosely and keep in a water-bath at 60° for two hours. Cool and determine the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 410 nm, using as the blank 10 ml of *water* treated in the same manner, Appendix 5.15 A. Calculate the content of $C_{22}H_{28}FO_8P$ from the *extinction* obtained by repeating the operation using *dexamethasone sodium phosphate R.S.* instead of the substance being examined, and from the declared content of $C_{22}H_{28}FO_8P$ in the *dexamethasone sodium phosphate R.S.*

Storage : Store in single-dose or multiple-dose, light-resistant containers, in a cool place.

Labelling : The label on the container states the strength in terms of the equivalent amount of dexamethasone phosphate in suitable dose-volume.

Dextran 40 Injection

Dextran 40 Intravenous Infusion

Category : Plasma substitute.

Description : Almost colourless, slightly viscous solution.

Standards : Dextran 40 Injection is a sterile solution, in Dextrose Injection, 5 per cent w/v, or in Sodium Chloride Injection, of dextrans of weight average molecular weight about 40,000 derived from the dextrans produced by the fermentation of sucrose by means of a suitable strain of *Leuconostoc mesenteroides*.

pH : Between 3.5 and 6.5 for solutions in Dextrose Injection. Between 4.0 and 7.0 for solutions in Sodium Chloride Injection, Appendix 5.10.

Acetone : To 10 ml add sufficient *ammonium sulphate* to give a saturated solution, add 1 ml of *sodium nitroprusside solution* and 5 ml of *strong ammonia solution*, and allow to stand for ten minutes. Any purple colour produced is not deeper than that produced by treating similarly 10 ml of a 0.02 per cent v/v solution of *acetone*.

Alcohol : Distil 100 ml, collect the first 45 ml of distillate, and dilute to 50 ml with *water*. Mix 10 ml of *0.1N potassium dichromate* and 10 ml of *sulphuric acid* in a stoppered boiling tube, immediately add 5 ml of the distillate, mix, stopper the tube, and allow to stand for five minutes. Transfer to a 500-ml flask, dilute to about 300 ml with *carbon dioxide-free water*, add 2 g of *potassium iodide* and 1 ml of a 10 per cent w/v solution of *potassium thiocyanate*, allow to stand for five minutes, and titrate the liberated iodine with *0.1N sodium thiosulphate*, using *starch solution* added towards the end of the titration, as indicator. Repeat the determination, beginning at the words "Mix 10 ml of *0.1N potassium dichromate* ..., but using 5 ml of *water* in place of 5 ml of the distillate. The difference between the titrations is not more than 4.2 ml"

Nitrogen : Carry out Method B for the *determination of nitrogen*, Appendix 3.3.5, using 50 ml; for solutions in Dextrose Injection, use 30 ml of *nitrogen-free sulphuric acid* and for solutions in Sodium Chloride Injection, 20 ml of *nitrogen-free sulphuric acid*; not more than 0.35 ml of *0.1N sulphuric acid* is required.

Content of dextrose : Between 4.5 and 5.5 per cent w/v for solution in Dextrose Injection when determined by the following method: Dilute 15.0 ml to 50.0 ml with *water*; to 5.0 ml in a stoppered flask add 25 ml of a buffer solution containing 14.3 per cent w/v of *sodium carbonate* and 4.0 per cent w/v of *potassium iodide*; and 25.0 ml of *0.1N iodine*, stopper the flask and allow to stand for exactly thirty minutes at 20°, add 30 ml of *dilute hydrochloric acid* and titrate immediately with *0.1N sodium thiosulphate*. Repeat the operation using 5 ml of *water* and beginning at the words "add 25 ml of a buffer solution ...", the difference between the titrations represents the amount of iodine required. Each ml of *0.1N iodine* is equivalent to a 0.00901 g of dextrose.

Molecular size : For solutions in Dextrose Injection, before proceeding with tests A and B, add four volumes of *alcohol*, centrifuge, and dissolve the residue in a volume of Sodium Chloride Injection sufficient to restore the original volume.

(A) Determine the *viscosity ratios* at 37° of solutions in *saline solution* containing about 3.5, 2.5, 1.5 and 0.75

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

per cent w/v of dextrans, accurately determined, Appendix 5.18. For each solution plot (viscosity ratio–1.00)/concentration in per cent w/v against concentration in per cent w/v. The intercept on the viscosity axis of the straight line joining the points represents the intrinsic viscosity; the intrinsic viscosity is between 0.16 and 0.20.

(B) Place in each of five stoppered flasks 100 ml of a solution in *saline solution* containing 6 per cent w/v of dextrans and add slowly with continuous stirring, sufficient *ethyl alcohol* to produce a faint cloudiness (about 45 ml is usually required). Add 0.5, 1.0, 1.5, 2.0 and 2.5 ml respectively of *ethyl alcohol*, stopper the flasks and immerse in a water-bath at about 35° with occasional shaking until clear solutions are obtained, transfer the flask to a water-bath maintained at 24.9° to 25.1° and allow to stand overnight or until two clear liquid phases are formed. Reject the supernatant liquids, dissolve separately the syrupy residues in sufficient *saline solution* to produce 25.0 ml, remove the alcohol by evaporation under reduced pressure, dilute to 25.0 ml with *water* and determine the *optical rotation*, Appendix 5.12. From the optical rotations calculate the amount of dextrans precipitated. Choose that fraction containing as nearly as possible but not more than 10 per cent of the dextrans present in the injection and determine the intrinsic viscosity by the method described above; the intrinsic viscosity is not more than 0.27.

(C) Place in each of four stoppered flasks 100 ml of a solution in *saline solution* containing 6 per cent w/v of dextrans and add slowly, with continuous stirring, 80, 90, 100 and 110 ml respectively of *ethyl alcohol*, stopper the flasks, transfer to a water-bath maintained at 24.9° to 25.1°, and allow to stand overnight or until two clear liquid phases are formed. Separate the supernatant solution from the syrupy residues. Remove the alcohol from each supernatant solution separately by evaporation under reduced pressure, dialyse in cellophane tubing against *water* to remove sodium chloride, adjust the volume to 25.0 ml with *water*, add sufficient *sodium chloride* to produce solutions containing 0.9 per cent w/v and determine the *optical rotation*, Appendix 5.12. From the optical rotations calculate the amounts of dextrans present. Choose that fraction containing as nearly as possible but not more than 10 per cent of the dextrans present in the injection and determine the intrinsic viscosity by the method described above; the intrinsic viscosity is not less than 0.08.

Foreign protein : Inject 0.5 ml on three occasions at intervals of two days into the peritoneal cavity of each of six healthy guinea-pigs weighing not less than 250 g which have not previously been treated with any material which will interfere with the test. Inject 0.2 ml intravenously into each of three of the guinea-pigs fourteen days after the first intra-peritoneal injection, and into each of the other three guinea-pigs twenty-one days after the first intra-peritoneal injection. Observe the guinea-pigs for thirty minutes after each intravenous injection and again twenty-four hours later; the animals exhibit no signs of anaphylaxis, such as coughing, bristling of hair, or respiratory distress.

Heavy metals : Not more than 5 parts per million, determined by Method A, Appendix 3.2.4, on 4 ml to which 5 ml of *dilute acetic acid* and sufficient *water* are added to produce 25 ml.

Pyrogens : Complies with the *test for pyrogens*, using not less than 10 ml per kg of the rabbit's weight, Appendix 2.36.

Sulphated ash : Not more than 0.05 per cent w/v, Appendix 3.2.7, after deducting sulphated ash due to the sodium chloride present, determined by titrating 25 ml with *0.1N silver nitrate*, using *potassium chromate solution* as indicator; each ml of *0.1N silver nitrate* is equivalent to 0.007102 g of sulphated ash.

Other requirements : Complies with the requirements stated under Injections.

Content of dextrans : Between 9.0 and 11.0 per cent w/v for solutions in Dextrose Injection and between 9.5 and 10.5 per cent w/v for solutions in Sodium Chloride Injection, determined by the following method : Add a drop of *dilute ammonia solution* and determine the *optical rotation*, Appendix 5.12. Calculate the content of dextrans from the following expressions : 0.5076 (α-0.528D) for solutions in Dextrose Injection and 0.5076 for solutions in Sodium Chloride Injection, where α is the observed angular rotation and D is the content of dextrose per cent w/v, determined by the method for **Content of dextrose.**

Storage : Store in a cool place; temperature fluctuations should be avoided.

Labelling : The label on the container states (1) the strength as the percentage w/v of dextrans; (2) the name of the solvent; (3) that the contents should not be used if they are hazy or a deposit is present; (4) the strain of *Leuconostoc mesenteroides* used; (5) the storage conditions.

Dextran 110 Injection

Dextran 110 Intravenous Infusion

Category : Plasma substitute.

Description : Almost colourless, slightly viscous solution.

Standards : Dextran 110 Injection is a sterile solution in Dextrose Injection, 5 per cent w/v, or in Sodium Chloride Injection, of dextrans of average molecular weight about 110,000 derived from the

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

dextrans produced by the fermentation of sucrose by means of a suitable strain of *Leuconostoc mesenteroides*.

pH : Between 3.5 and 6.5 for solutions in Dextrose Injection. Between 5.0 and 7.0 for solutions in Sodium Chloride Injection, Appendix 5.10.

Acetone; Alcohol; Nitrogen; Content of dextrose; Heavy metals; Sulphated ash; Foreign protein; Pyrogens : Complies with the tests described under Dextran 40 Injection.

Molecular size : For solutions in Dextrose Injection, before proceeding with tests (A) and (B), add four volumes of *alcohol*, centrifuge, and dissolve the residue in a volume of Sodium Chloride Injection equivalent to the original volume.

(A) Determine the *viscosity ratios*, at 37°, of solutions in *saline solution* containing about 2.0, 1.0, 0.5 and 0.25 per cent w/v of dextrans, accurately determined, Appendix 5.18. For each solution plot (viscosity ratio − 1.00)/concentration in per cent w/v against concentration in per cent w/v. The intercept on the viscosity axis of the straight line joining the points represents the intrinsic viscosity; the intrinsic viscosity is not less than 0.27 and not more than 0.32.

(B) Place 100 ml in each of five stoppered flasks and adjust the temperature to 24.9° to 25.1°C. With precautions to maintain this temperature, add slowly with continuous stirring, sufficient *ethyl alcohol* to produce a faint cloudiness (about 45 ml is usually required). Add 0.5, 1.0, 1.5, 2.0 and 2.5 ml respectively of *ethyl alcohol*, stopper the flasks, and immerse in a water-bath at about 35° with occasional shaking until clear solutions are obtained. Transfer the flasks to a water-bath maintained at 24.9° to 25.1° and allow to stand overnight or until two clear liquid phases are formed. Reject the supernatant liquids, dissolve separately the syrupy residues in sufficient *saline solution* to produce 25.0 ml, remove the alcohol by evaporation under reduced pressure, dilute to 25.0 ml with *water*, and determine the *optical rotation*, Appendix 5.12. From the optical rotations, calculate the amounts of dextran precipitated. Choose those fractions containing as nearly as possible but not more than 10 per cent of the dextrans present in the injection and determine the intrinsic viscosity by the method described above; the intrinsic viscosity is not more than 0.40.

(C) Complies with the *test for urinary excretion of dextrans*, Appendix 2.34.

Other requirements : Complies with the requirements stated under Injections.

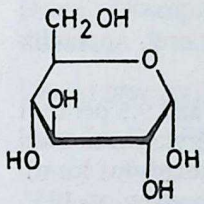
Content of dextrans : Between 5.5 and 6.5 per cent w/v determined as described under Dextran 40 Injection.

Storage : Store in a cool place; temperature fluctuations should be avoided. Dextran 110 injection in Sodium Chloride Injection may be stored at temperature not exceeding 40°

Labelling : The label on the container states (1) the strength as the percentage w/v of dextrans; (2) the name of the solvent; (3) that the contents should not be used if they are hazy or contain any suspended matter; (4) the strain of *Leuconostoc mesenteroides* used; (5) the storage conditions.

Dextrose

Glucose



$C_6H_{12}O_6$ Mol. Wt. 180.16 (anhydrous)

$C_6H_{12}O_6, H_2O$ Mol. Wt. 198.17 (monohydrate)

Category : Nutrient.

Description : White or cream-coloured, crystalline or granular powder; odourless; taste, sweet.

Solubility : Freely soluble in *water*; sparingly soluble in boiling *alcohol*; very soluble in boiling *water*.

Standards : Dextrose is α-D-glucopyranose. It is a sugar usually obtained by the hydrolysis of starch. It is anhydrous or contains one molecule of water of crystallisation.

Identification : (A) To 5 ml of a 1 per cent w/v solution, add 2 ml of *2N sodium hydroxide* and 0.05 ml of *copper sulphate solution*; the solution is blue and clear. Heat to boiling; a copious red precipitate is formed.

(B) When heated, it melts, swells up and burns, and an odour of burnt sugar is perceptible.

Specific optical rotation : Between +52.5° and +53.0°, calculated on anhydrous basis, determined in a 10 per cent w/v solution containing 0.2 ml of *dilute ammonia solution*, Appendix 5.12.

Acidity : Dissolve 6 g in 25 ml of *carbon dioxide-free water* and add 0.25 ml of *dilute phenolphthalein solution*; the solution is colourless. Not more than 0.15 ml of *0.1N sodium hydroxide* is required to produce a pink colour.

Less soluble sugars and dextrins : Dissolve 1 g in 30 ml of boiling *alcohol (90 per cent)*; a clear solution is

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

obtained which does not produce any deposition on cooling.

Arsenic : Not more than 1 part per million, Appendix 3.2.1.

Heavy metals : Not more than 5 parts per million, determined by Method A, Appendix 3.2.4, on a solution prepared by dissolving 4 g in 10 ml of *water*, 2 ml of *dilute acetic acid* and sufficient *water* to produce 25 ml.

Chloride : 1 g complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphate : 5 g complies with the *limit test for sulphates*, Appendix 3.2.8.

Sulphites : To 20 ml of a 10 per cent w/v solution, add 0.05 ml of *0.1N iodine* and one drop of *starch solution;* a blue colour develops.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Between 7.5 per cent and 9.5 per cent (hydrous form), determined on 1.0 g by drying in an oven at 105°; not more than 0.5 per cent (anhydrous form), determined on 2.0 g by drying in an oven at 105°, Appendix 5.8.

Dextrose intended for parenteral administration complies with the following additional requirements :

Description : White crystalline or granular powder.

Clarity and colour of solution : Dissolve 25.0 g in sufficient *water* to produce 50.0 ml. The solution is clear and is not more intensely coloured than a solution prepared by mixing 1.0 ml of *cobalt chloride C.S.*, 3.0 ml of *ferric chloride C.S.* and 2.0 ml of *copper sulphate C.S.* and sufficient *water* to produce 10.0 ml and diluting 3.0 ml of this solution with *water* to 50.0 ml.

Storage : Store in tightly-closed containers.

Dextrose Injection

Dextrose Intravenous Infusion

Category : Fluid and nutrient replenisher.

Usual strengths : 5.0 per cent w/v, 10.0 per cent w/v, 25.0 per cent w/v and 50.0 per cent w/v.

Description : Clear, colourless liquid; an Injection containing 25.0 per cent w/v or more of dextrose; may be not more than faintly straw-coloured.

Standards : Dextrose Injection is a sterile solution of Dextrose in Water for Injection. It contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of anhydrous dextrose, $C_6H_{12}O_6$.

Identification : Complies with **Identification** test (A) described under Dextrose.

pH : Between 3.5 and 6.5, Appendix 5.10.

Heavy metals : Not more than 5 parts per million, determined by Method A, Appendix 3.2.4, on a solution prepared by evaporating a volume of injection equivalent to 4 g of dextrose to 10 ml, and adding 2 ml of *dilute acetic acid* and sufficient *water* to produce 25 ml.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using a quantity containing not less than 0.5 g of dextrose, $C_6H_{12}O_6$ per kg of the rabbit's weight.

5-Hydroxymethylfurfural and related substances : Dilute a volume equivalent to 1.0 g of dextrose, $C_6H_{12}O_6$, to 250.0 ml with *water* and measure the *extinction* of the resulting solution at the maximum at about 284 nm, Appendix 5.15A; the *extinction* is not more than 0.25.

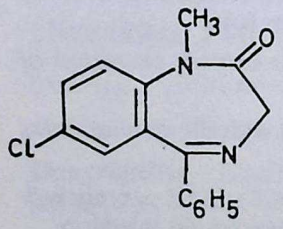
Other requirements : Complies with the requirements stated under Injections.

Assay : Measure accurately a volume equivalent to between 2 g and 5 g of anhydrous dextrose, $C_6H_{12}O_6$, and transfer to a 100-ml volumetric flask. Add 0.2 ml of *dilute ammonia solution* and add *water* to volume; mix well and set aside for thirty minutes and measure the *optical rotation* in a 200-mm tube, Appendix 5.12. The observed rotation in degrees multiplied by 0.9477 represents the weight in g of dextrose, $C_6H_{12}O_6$ in the volume taken for assay.

Storage : Store in single-dose containers in a cool place.

Labelling : The label on the container states (1) the strength as the percentage w/v of anhydrous dextrose, $C_6H_{12}O_6$; (2) the storage conditions; (3) the date after which the Injection is not intended to be used; (4) that the Injection should not be used if it contains visible solid particles.

Diazepam



$C_{16}H_{13}ClN_2O$ Mol. Wt. 284.74

Category : Anticonvulsant; sedative.

Dose : 5 to 30 mg daily, in divided doses.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Description : White or almost white to pale-yellow, crystalline powder; odourless, or almost odourless; tasteless at first, followed by bitter taste.

Solubility : Sparingly soluble in *water*; soluble in *alcohol*, freely soluble in *chloroform*.

Standards : Diazepam is 7-chloro-1, 3-dihydro-1-methyl-5-phenyl-2-*H*-1, 4-benzediazepin-2-one. It contains not less than 98.5 per cent and not more than the equivalent of 101.0 per cent of $C_{16}H_{13}ClN_2O$, calculated with reference to the dried substance.

Identification : (A) Protect the solution from light and measure the *extinction* immediately. The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.0005 per cent w/v solution in *0.1N hydrochloric acid* exhibits two maxima, at 241 nm and 286 nm; *extinction* at 241 nm, about 0.5 and at 286 nm, about 0.24, Appendix 5.15 A.

(B) Protect the solution from light and measure the *extinction* immediately. The light absorption, in the range 325 to 400 nm, of a 1-cm layer of a 0.0015 per cent w/v solution in *0.1N hydrochloric acid* exhibits a maximum only at 362 nm; *extinction* at 362 nm, about 0.22, Appendix 5.15 A.

(C) Carry out the *oxygen-flask method*, Appendix 3.3.6, using 20 mg and 5 ml of *dilute sodium hydroxide solution* as the absorbing liquid. When the process is complete, acidify the solution with *dilute sulphuric acid* and boil gently for two minutes; the solution gives the reactions of *chlorides*.

Melting range : Between 131° and 135°, Appendix 5.11.

Heavy metals : Not more than 10 parts per million, determined on 2.0 g by Method B, Appendix 3.2.4.

Decomposition products : Carry out in subdued light the method for *thin-layer chromatography*, Appendix 5.4.3, using a suitable *silica gel GF 254* as the coating substance and a mixture of 20 volumes of *hexane* and 20 volumes of *ethyl acetate* as the mobile phase. Apply separately to the plate 5 µl of each of two solutions, freshly prepared in *acetone* containing (1) 10.0 per cent w/v of the substance being examined and (2) 0.01 per cent w/v of the substance being examined. After removal of the plate, allow it to dry in air and examine under an ultra-violet lamp having a maximum output at about 254 nm. Any spot in the chromatogram obtained with solution (1) other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (2).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying "in vacuo at 60°" for four hours, Appendix 5.8.

Assay : Weigh accurately about 0.5 g, dissolve in 80 ml of *glacial acetic acid* with the aid of heat, if necessary, cool, and titrate with *0.1N perchloric acid*, determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02847 g of $C_{16}H_{13}ClN_2O$.

Storage : Store in tightly-closed, light-resistant containers.

Diazepam Capsules

Category : Anticonvulsant; sedative.

Dose : Diazepam, 5 to 30 mg daily, in divided doses.

Usual strengths : 5 mg; 10 mg.

Standards : Diazepam Capsules contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Diazepam, $C_{16}H_{13}ClN_2O$.

Identification : (A) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using a suitable silica gel as the coating substance and a mixture of 10 volumes of *chloroform* and 1 volume of *methyl alcohol* as the mobile phase. Apply separately to the plate, 2 µl of each of two solutions in *methyl alcohol*. For solution (1) shake a quantity of the contents of the capsules with sufficient *methyl alcohol* to produce a solution containing the equivalent of 5 mg of Diazepam per ml, allow to settle, and decant the supernatant liquid. Solution (2) is a 0.5 per cent w/v solution of *diazepam R.S.* After removal of the plate, spray it with a 10 per cent v/v solution of *sulphuric acid* in *alcohol* and heat at 105° for ten minutes. The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

(B) The light absorption, in the range 230 to 250 nm, of a 1-cm layer of the solution obtained in the **Assay**, exhibits two maxima at 242 and 284 nm, Appendix 5.15 A.

Other requirements : Comply with the requirements stated under Capsules.

Assay : Weigh accurately a quantity of the mixed contents of 20 capsules equivalent to about 10 mg of Diazepam, add 5 ml of *water*, mix, and allow to stand for fifteen minutes. Add 90 ml of a 0.5 per cent w/v solution of *sulphuric acid* in *methyl alcohol*, shake for fifteen minutes, and add sufficient of the *sulphuric acid solution* to produce 100.0 ml and filter. Dilute 10.0 ml of the filtrate to 100.0 ml with the same solution. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 284 nm, Appendix 5.15 A. Calculate the content of $C_{16}H_{13}ClN_2O$, taking 446 as the value of E(1 per cent, 1-cm) at the maximum at about 284 nm.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Storage : Store in light-resistant containers.

Diazepam Injection

Category : Tranquilliser.

Dose : Diazepam, intramuscular or intravenous injection, 2 to 10 mg repeated in two to four hours if necessary.

Usual strength : 5 mg per ml.

Description : Clear, colourless or almost colourless solution.

Standards : Diazepam Injection is a sterile solution of Diazepam in a suitable medium. It contains not less than 90.0 per cent and not more than 110.0 per cent of the labelled amount of $C_{16}H_{13}ClN_2O$.

Identification : (A) Complies with **Identification** test (A) described under Diazepam Capsules, using as solution (1), a volume equivalent to 5 mg of Diazepam.

(B) The light absorption, in the range 230 to 350 nm of the solution obtained in the **Assay**, exhibits two maxima at 242 nm and 284 nm, Appendix 5.15 A.

pH : Between 6.2 and 6.9, Appendix 5.10.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using a volume equivalent to 0.25 mg of Diazepam per kg of the rabbit's weight.

Other requirements : Complies with the requirements stated under Injections.

Assay : To an accurately measured volume equivalent to about 10 mg of Diazepam, add 20 ml of *buffer solution, pH 7.0* and extract with four quantities, each of 20 ml of *chloroform*, passing each extract through about 5 g of *anhydrous sodium sulphate*; dilute the combined chloroform extracts to 100.0 ml with *chlorofom*. Pipette 10 ml of this solution and evaporate to dryness under *nitrogen*; add sufficient volume of 0.5 per cent w/v solution of *sulphuric acid* in *methyl alcohol* to produce 100.0 ml; measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 284 nm, Appendix 5.15 A. Calculate the content of $C_{16}H_{13}ClN_2O$, taking 446 as the value of E(1 per cent, 1-cm) at the maximum at about 284 nm.

Storage : Store in a single-dose or multiple dose light-resistant containers.

Diazepam Tablets

Category : Sedative.

Dose : Diazepam, 5 to 30 mg daily; in divided doses.

Usual strengths : 2 mg; 5 mg; 10 mg.

Standards : Diazepam Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of stated amount of Diazepam, $C_{16}H_{13}ClN_2O$.

Identification : (A) Comply with **Identification** test (A) described under Diazepam Capsules, when solution (1) is prepared from the powdered tablets.

(B) The light absorption, in the range 230 to 350 nm, of the solution obtained in the **Assay**, exhibits two maxima, at 242 nm and 284 nm, Appendix 5.15 A.

Uniformity of content : Powder one tablet, add 5 ml of *water*, mix and allow to stand for fifteen minutes. Add 90 ml of a 0.5 per cent w/v solution of *sulphuric acid* in *methyl alcohol*, shake for fifteen minutes, add sufficient sulphuric acid solution to produce 100.0 ml and filter. Dilute a volume of the filtrate equivalent to about 1 mg of Diazepam to 100.0 ml with the *sulphuric acid solution* and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 284 nm, Appendix 5.15 A. Calculate the content of $C_{16}H_{13}ClN_2O$ in the tablet, taking 446 as the value of E(1 per cent, 1-cm) at the maximum at about 284 nm.

Repeat the operation with a further nine tablets. The content of each tablet is between 90 per cent and 110 per cent of the average except that for one tablet the content may be between 85 per cent and 115 per cent of the average.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 10 mg of Diazepam, add 5 ml of *water*, mix and allow to stand for fifteen minutes. Add 90 ml of a 0.5 per cent w/v solution of *sulphuric acid* in *methyl alcohol*, shake for fifteen minutes, and add sufficient of the sulphuric acid solution to produce 100.0 ml and filter. Dilute 10.0 ml of the filtrate to 100.0 ml with the same solution and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 284 nm, Appendix 5.15 A. Calculate the content of $C_{16}H_{13}ClN_2O$, taking 446 as the value of E(1 per cent, 1-cm) at the maximum at about 284 nm.

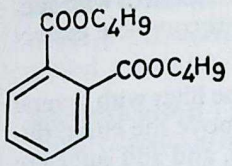
Storage : Store in light-resistant containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Dibutyl Phthalate

n-Butyl Phthalate



$C_{16}H_{22}O_4$ Mol. Wt. 278.35

Category : Insect repellent.

Description : Clear, colourless or faintly coloured liquid, odourless or has a faint odour.

Solubility : Very slightly soluble in *water*; miscible with *alcohol* and with *solvent ether.*

Standards : Dibutylphthalate is di(*n*-butyl) benzene-1, 2-dicarboxylate. It contains not less than 99.0 per cent w/v of $C_{16}H_{22}O_4$.

Identification : Boil gently 1 g with 5 ml of *alcoholic potassium hydroxide solution* for about ten minutes. Add 5 ml of *water* and evaporate the mixture to half its volume, cool, add 1 ml of *hydrochloric acid*, filter, dry the precipitate and melt in a small tube; add 0.5 g *resorcinol* and one drop of *chloroform*. Heat to about 180° for three minutes. Cool, add 1 ml of *sodium hydroxide solution* and pour in *water*; an intense yellowish-green fluorescence is produced.

Boiling range : About 330°, Appendix 5.3.

Acidity : Mix 20 ml with 50 ml of *alcohol*, previously neutralised to *phenolphthalein solution*. The solution requires for neutralisation not more than 6.2 ml of *0.01N sodium hydroxide, phenolphthalein solution* being used as indicator.

Wt. per ml : Between 1.042 g and 1.049 g, Appendix 5.19.

Refractive index : Between 1.492 and 1.495, Appendix 5.14, determined at 20°.

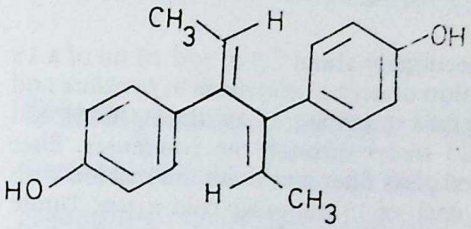
Refractive index : Between 1.492 and 1.495 determined at 20°, Appendix 5.14.

Water : Mix 1 volume with 19 volumes of *carbon disulphide* at 15°, no opalescence is produced.

Assay : Carry out the method for the *determination of esters*, Appendix 3.3.2, using about 1.5 g, accurately weighed and 50.0 ml of *0.5N alcoholic potassium hydroxide*. Each ml of *0.5N alcoholic potassium hydroxide* is equivalent to 0.06959 g of $C_{16}H_{22}O_4$.

Dienoestrol

Dehydrostilbestrol; Dienoestrol



$C_{18}H_{18}O_2$ Mol. Wt. 226.33

Category : Estrogen.

Dose : In the treatment of menopausal symptoms, 0.5 to 5 mg daily.

In the treatment of carcinoma of the prostate and mammary carcinoma, 15 to 30 mg daily.

Description : Colourless or white, needle-like crystals or white, crystalline powder; odourless.

Solubility : Practically insoluble in *water*; freely soluble in *alcohol*, and in *acetone*; insoluble in *solvent ether*; slightly soluble in *chloroform.*

Standards : Dienoestrol is (*Z*, *Z*)-4, 4′-(1,2-diethylidene-1, 2-ethanediyl) bisphenol. It contains not less than 98.5 per cent and not more than the equivalent of 101.5 per cent of $C_{18}H_{18}O_2$, calculated with reference to the dried substance.

Identification : (A) Dissolve 10 mg in 0.5 ml of *alcohol*, add 1 ml of *hydrochloric acid* and about 50 mg of *vanillin*; a blue colour is produced immediately; dilute with *water*; the colour persists; add an alkali, the colour disappears (distinction from diethylstilboestrol which will produce no colour).

(B) Dissolve 1 mg in 5 ml of *glacial acetic acid*, add 1 ml of a 1 per cent v/v solution of *bromine* in *glacial acetic acid*, allow to stand for thirty seconds and divide into two parts :

(a) To one part add one drop of *liquefied phenol* and heat in a water-bath for two minutes; an emerald green colour develops. Add a few mg of sucrose and continue the heating in the water-bath; the green colour changes through deep blue and grey to straw colour and finally to reddish-brown.

(b) Heat the other part in a water-bath for two minutes. To 0.5 ml of this solution in a dry test-tube add 0.5 ml of *ethyl alcohol*, mix and add 10 ml of *water*; a reddish-violet colour is produced. Add 5 ml of *chloroform*, and shake vigorously and set aside for ten minutes; the lower layer is coloured deep orange-red and the upper layer is almost colourless.

Melting range : Between 232° and 235°, Appendix 5.11.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.2 per cent , determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 1.5 g, add 10 ml of a 15 per cent v/v solution of *acetic anhydride* in *pyridine* and heat under reflux on a water-bath for two hours. Cool, add 50 ml of ice-cold *water* through the condenser, filter through a sintered-glass filter and wash the residue with three quantities, each of 15 ml, of ice-cold *water*. Titrate the combined filtrate and washings slowly and with vigorous shaking with *0.5N sodium hydroxide* using *phenolphthalein solution* as indicator, until the red colour presists for 10 seconds. Perform a blank determination and make any necessary correction. Each ml of *0.5N sodium hydroxide* is equivalent to 0.06659 g of $C_{18}H_{18}O_2$.

Storage : Store in well-closed, light-resistant containers.

Dienoestrol Tablets

Dehydrostilbestrol Tablets

Category : Estrogen.

Dose : Dienoestrol. In the treatment of menopausal symptoms, 0.5 to 5 mg daily. For the suppression of lactation, 15 mg thrice daily for three days, followed by 15 mg daily for six days.

Usual strength : 1 mg.

Standards : Dienoestrol Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Dienoestrol, $C_{18}H_{18}O_2$.

Identification : Extract a quantity of the powdered tablets equivalent to about 15 mg of Dienoestrol with *solvent ether* and evaporate to dryness. The residue complies with the **Identification** tests (A) and (B) described under Dienoestrol.

Uniformity of content : Powder one tablet and extract with successive quantities of *solvent ether* until complete extraction is effected. Combine the ether extracts and evaporate to dryness. Dissolve the residue in 10 ml of *alcohol* and add sufficient *water* to produce 20.0 ml. Complete the test as described in the **Assay** beginning at the words "To 10.0 ml add 2 ml of *dilute hydrochloric acid* ....". From the *extinction* obtained calculate the content of $C_{18}H_{18}O_2$ in the tablet. Repeat the operation with a further 9 tablets and calculate the average content of the ten tablets. The content of each tablet is between 90 per cent and 110 per cent of the average except that for one tablet the content may be between 85 per cent and 115 per cent of the average.

Other requirements : Comply with the requirements stated under Tablets.

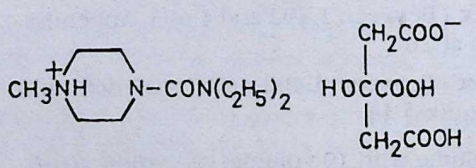
Assay : Weigh and powder 20 tablets. Triturate a quantity of the powder equivalent to 5 mg of Dienoestrol with successive quantities of *solvent ether* until complete extraction is effected.

Filter the ether solution and wash the filter with several small quantities of *solvent ether*. Remove the ether, dissolve the residue in 50 ml of *alcohol*, and add sufficient *water* to produce 100.0 ml. To 10.0 ml add 2 ml of *dilute hydrochloric acid*, 4 ml of *sodium molybdophosphotungstate solution*, and 50 ml of *water* and allow to stand for ten minutes. Add 10 ml of a 25 per cent w/v solution of *anhydrous sodium carbonate* and sufficient *water* to produce 100.0 ml, mix thoroughly, and allow to stand for one hour. If the solution is hazy or contains a precipitate, transfer a suitable volume to a stoppered centrifuge tube and add a quarter of this volume of *solvent ether*. Shake, centrifuge, and reject the upper layer, including any precipitate which has collected at the interface. Measure the *extinction* of a 1-cm layer of the resulting solution at 750 nm, Appendix 5.15 A, using as the blank solution prepared in a similar manner but omitting the powdered tablets.

Repeat the operation using a solution of 5 mg of *dienoestrol R.S.*, 50 ml of *alcohol* and sufficient *water* to produce 100.0 ml and beginning at the words "To 10.0 ml add 2 ml of *dilute hydrochloric acid* ....". From the *extinction* so obtained calculate the content of $C_{18}H_{18}O_2$ in the tablets.

Storage : Store in well-closed, light-resistant containers.

Diethylcarbamazine Citrate



$C_{10}H_{21}N_3O, C_6H_8O_7$ Mol. Wt. 391.42

Category : Antifilarial; Anthelmintic.

Dose : 150 mg to 500 mg daily.

Description : White, crystalline, powder; odourless or has a slight odour; taste, acid, bitter. Slightly hygroscopic.

Solubility : Very soluble in *water*; sparingly soluble in *alcohol*; practically insoluble in *chloroform* and in *solvent ether*.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Standards : Diethylcarbamazine Citrate is 4-diethylcarbamoyl-1-methylpiperazinium dihydrogen citrate. It contains not less than 98.0 per cent and not more than the equivalent of 100.5 per cent of $C_{10}H_{21}N_3O, C_6H_8O_7$, calculated with reference to the dried substance.

Identification : (A) Dissolve 0.5 g in 10 ml of *water* and 10 ml of *sodium hydroxide solution* and extract with four quantities, each of 5 ml, of *chloroform* (set aside the aqueous layer). Wash the combined chloroform extracts with *water*, filter through a plug of cotton and remove the chloroform from the filtrate by evaporation. To the residue add 1 ml of *ethyl iodide* and gently reflux for five minutes. Cool, separate the viscous yellow oil and dissolve it in a small volume of *alcohol*. Chill the alcohol solution in an ice-bath, and with continuous stirring, add sufficient *solvent ether* to precipitate the quaternary salt, and stir until the salt crystallises. After the mixture has remained in ice for thirty minutes, filter; the precipitate, after drying at 105° melts at about 152°, Appendix 5.11.

(B) Neutralise the aqueous layer set aside in the **Identification** test A with *dilute sulphuric acid*, add excess of *mercuric sulphate solution*, boil, and add 0.2 ml of *potassium permanganate solution*; a white precipitate is produced.

Melting range : Between 135° and 138°, Appendix 5.11.

Heavy metals : Not more than 20 parts per million, determined by Method A, Appendix 3.2.4, on a solution prepared by dissolving 1.0 g in 20 ml of *water*, 0.5 ml of *0.1N hydrochloric acid* and sufficient *water* to produce 25 ml.

N-Methylpiperazine : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 6 volumes of *alcohol*, 3 volumes of *glacial acetic acid*, and 1 volume of *water* as the mobile phase. Apply separately to the plate 5 µl of each of two solutions in *methyl alcohol* containing (1) 5.0 per cent w/v of the substance being examined and (2) 0.005 per cent w/v of *N-methylpiperazine R.S.* After removal of the plate, allow it to dry in air, and spray with a mixture of 3 volumes of a 10 per cent w/v solution of *platinic chloride*, 97 volumes of *water*, and 100 volumes of a 6 per cent w/v solution of *potassium iodide*. The spot in the chromatogram obtained with solution (2) is more intense than any corresponding spot in the chromatogram obtained with solution (1).

Sulphated ash : Not more than 0.1 per cent , Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.75 g and dissolve in 50 ml of *glacial acetic acid*, warming slightly to effect solution. Cool to 25° and titrate with *0.1N perchloric acid*, using *crystal-violet solution* as indicator. Perform a blank titration and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.03914 g of $C_{10}H_{21}N_3O, C_6H_8O_7$.

Storage : Store in tightly-closed containers.

Diethylcarbamazine Tablets

Diethylcarbamazine Citrate Tablets

Category : Antifilarial; anthelmintic.

Dose : Diethylcarbamazine Citrate, 150 to 500 mg daily.

Usual strengths : 50 mg; 100 mg.

Standards : Diethylcarbamazine Tablets contain not less than 93.0 per cent and not more than 107.0 per cent of the stated amount of Diethylcarbamazine Citrate, $C_{10}H_{21}N_3O, C_6H_8O_7$.

Identification : Extract a quantity of the powdered tablets equivalent to about 0.5 g of Diethylcarbamazine Citrate with 2.5 ml of *water* and filter the extract into a separator. The filtrate complies with **Identification** test (A) described under Diethylcarbamazine Citrate.

N-Methylpiperazine : Comply with the test described under Diethylcarbamazine Citrate using as solution (1) a solution prepared by shaking a quantity of the powdered tablets equivalent to 0.5 g Diethylcarbamazine Citrate with 10 ml of *methyl alcohol* and filtering.

Other requirements : Comply with the requirements stated under Tablets.

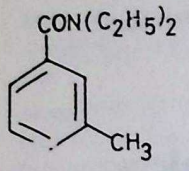
Assay : Weigh 20 tablets and reduce to a fine powder. Weigh accurately a quantity of the powder equivalent to about 0.75 g of Diethylcarbamazine Citrate, dissolve as completely as possible in a mixture of 10 ml of *water* and 10 ml of *5N sodium hydroxide* and extract with four quantities, each of 20 ml, of *chloroform*, washing each extract with the same two quantities, each of 20 ml, of *water*, and with a third quantity if the second becomes alkaline to *phenolphthalein solution*. Extract the combined chloroform extracts in succession with 25.0 ml of *0.1N sulphuric acid* and 15 ml and 10 ml of *water*. Combine the acid and water extracts, warm to remove chloroform, cool, and titrate the excess of acid with *0.1N sodium hydroxide*, using *bromocresol green solution* as indicator. Each ml of *0.1N sulphuric acid* is equivalent to 0.03914 g of $C_{10}H_{21}N_3O, C_6H_8O_7$.

Storage : Store in tightly-closed containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Diethyltoluamide



$C_{12}H_{17}NO$ Mol. Wt. 191.27

Category : Insect repellent.

Description : Colourless or faintly yellow liquid; odourless or almost odourless.

Solubility : Practically insoluble in *water* and in *glycerin*; miscible with *alcohol*, with *isopropyl alcohol* with *solvent ether*, and with *chloroform*.

Standards : Diethyltoluamide is *N*, *N*-diethyl-*m*-toluamide. It contains not less than 95.0 per cent and not more than the equivalent of 103.0 per cent w/v of $C_{12}H_{17}NO$, calculated with reference to the anhydrous substance.

Identification : (A) Heat 2 ml with 25 ml of 50 per cent v/v solution of *hydrochloric acid* under a reflux condenser for one hour. Make the mixture alkaline with *sodium hydroxide solution*, cool and extract with three quantities, each of 30 ml, of *solvent ether*. Reserve the aqueous layer. Evaporate the ether, dissolve the residue in 5 ml of *dilute hydrochloric acid*, cool to 5°, and add 5 ml of *sodium nitrite solution*. Allow to stand for ten minutes at 5°, add 10 ml of *water*, and extract with 20 ml of *solvent ether*. Evaporate the ether, add 1.0 g of *phenol* to the residue, cool and add 1 ml of *sulphuric acid*; an intense green colour is produced, which becomes red on pouring into *water* and green on making alkaline with *dilute sodium hydroxide solution*.

(B) Acidify the aqueous layer reserved in **Identification** test A, extract with two quantities, each of 20 ml of *solvent ether*, and evaporate the ether from the combined extracts. The residue, after drying at 60°, melts at about 108°, Appendix 5.11.

Refractive index : Between 1.520 and 1.524, Appendix 5.14.

Wt. per ml : Between 0.997 and 1.000 g determined at 20°, Appendix 5.19.

Acidity : 10.0 g dissolved in 50 ml of *alcohol* previously neutralised to *phenolphthalein solution*, requires for neutralisation not more than 4 ml of *0.01N sodium hydroxide*, using *phenolphthalein solution* as indicator.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

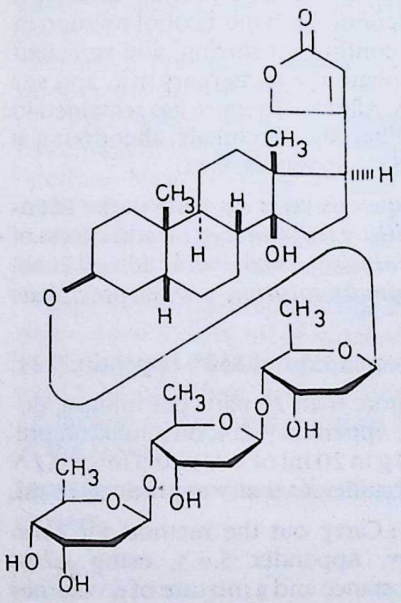
Water : Not more than 0.5 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately about 0.3 g, add 7 ml *nitrogen-free sulphuric acid* and carry out the *determination of nitrogen*, Appendix 3.3.5, using *0.1N sulphuric acid*. Each ml of *0.1N sulphuric acid* used is equivalent to 0.01913 g of $C_{12}H_{17}NO$.

Storage : Store in tightly-closed, dry containers.

CAUTION—It is irritant to eyes and mucous membranes.

Digitoxin



$C_{41}H_{64}O_{13}$ Mol. Wt. 764.95

Category : Cardiotonic.

Dose : Initial dose, 1 to 1.5 mg, divided over twenty-four to forty-eight hours; maintenance, 0.05 to 0.2 mg daily.

Description : White or almost white powder; odourless.

Solubility : Practically insoluble in *water*; sparingly soluble in *alcohol* and in *chloroform*; very slightly soluble in *solvent ether*.

Standards : Digitoxin is 3β [(O-2, 6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-O-2, 6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-2, 6-dideoxy-β-D-*ribo*-hexopyranosyl)-oxy]-14-hydroxy-5β, 14β-card-20(22)-enolide. It contains not less than 95.0 per cent and not more than the equivalent to 105.0 per cent of $C_{41}H_{64}O_{13}$, calculated with reference to the dried substance.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Identification : (A) Dissolve about 1 mg in 2 ml of *glacial acetic acid* with the aid of gentle heat, cool and add one drop of *ferric chloride test solution*, cautiously add 1 ml of *sulphuric acid* under the two liquids without mixing. A brown ring develops at the interface which gradually becomes blue and finally the acetic acid layer acquires a blue colour.

(B) Suspend about 0.5 g in ten drops of *alcohol (60 per cent)*. On treating with five drops of *dinitrobenzoic acid solution* and two drops of *dilute sodium hydroxide solution*, the suspension turns violet.

(C) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *kieselguhr G* as the coating substance, and a mixture of 50 volumes of *xylene*, 50 volumes of *ethyl methyl ketone* and 4 volumes of *formamide* as the mobile phase. Impregnate the prepared plate by allowing it to stand in a layer 5-mm deep of a mixture of 10 volumes of *formamide* and 90 volumes of *acetone* in a closed chamber until the solvent has ascended at least 15 cm. Remove the plate from the chamber and allow to stand for at least five minutes. Use the plate within two hours of impregnation.

Apply separately to the plate 3 µl of each of two solutions in a mixture of equal volumes of chloroform and *methyl alcohol* containing (1) 0.1 per cent w/v of the substance being examined and (2) 0.1 per cent w/v of *digitoxin R.S.* After removal of the plate, allow it to dry in an oven at 115° for twenty minutes. Cool and spray with a mixture of 15 volumes of a solution of 25 g of *trichloroacetic acid* in 100 ml of *alcohol* and 1 volume of a freshly prepared 3 per cent w/v solution of *chloramine T* and heat at 115° for five minutes. Examine under an ultra-violet lamp. The principal spot in the chromatogram obtained with solution (1) corresponds to the spot in the chromatogram obtained with solution (2).

(D) Dissolve 0.5 g in sufficient *alcohol-free chloroform* to produce 20 ml; *specific optical rotation*, about +18°, calculated on the undried material, Appendix 5.12.

Clarity of solution : Dissolve 0.1 g in 5 ml of *chloroform* in a tightly-stoppered cylinder and keep aside for twenty-four hours. A solution with not more than a slight opalescence is obtained.

Digitonin : Dissolve 10 mg in 2 ml of *alcohol* in a test-tube, the inner walls of which are free from scratches; add 2 ml of a 0.5 per cent w/v solution of *cholesterol* in *alcohol* and mix by gentle agitation; no precipitate is formed within ten minutes.

Gitoxin : Not more than 4 per cent, determined by the following method : Weigh accurately about 50 mg and dissolve in sufficient of a mixture of equal volumes of *chloroform* and *methyl alcohol* to produce 10.0 ml. Dilute 1.0 ml to 25.0 ml with a mixture of equal volumes of *hydrochloric acid* and *glycerol* and allow to stand for one hour. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 352 nm, Appendix 5.15 A, using as the blank a mixture of equal volumes of *hydrochloric acid* and *glycerol*. Calculate the content of gitoxin from the *extinction* obtained by repeating the test on 1 ml of a 0.02 per cent w/v solution of *gitoxin R.S.* in a mixture of equal volumes of *chloroform* and *methyl alcohol*.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.5 per cent, determined on 0.1 g by drying "in vacuo", Appendix 5.8.

Assay : Weigh accurately about 40 mg and dissolve in sufficient *alcohol* to produce 50.0 ml. Dilute 5.0 ml of this solution to 100.0 ml with *alcohol* and mix. To 5.0 ml add 3.0 ml of *alkaline picric acid solution* and allow to stand for thirty minutes, protected from bright light. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 495 nm, Appendix 5.15 A, using as the blank 5.0 ml of *alcohol* and 3.0 ml of *alkaline picric acid solution*. Calculate the content of $C_{41}H_{64}O_{13}$ from the *extinction* obtained by repeating the **Assay** using *digitoxin R.S.* in place of the substance being examined, and from the declared content of $C_{41}H_{64}O_{13}$ in *digitoxin R.S.*

Storage : Store in well-closed, light-resistant containers.

Digitoxin Tablets

Category : Cardiotonic.

Dose : Digitoxin. Initial dose, 1.5 mg, divided over twenty-four to forty-eight hours; maintenance, 0.1 mg daily.

Usual strengths : 0.1 mg; 0.2 mg.

Standards : Digitoxin Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Digitoxin, $C_{41}H_{64}O_{13}$.

Identification : The powdered tablets comply with **Identification** test (A) described under Digitoxin.

Uniformity of content : Shake 1 tablet with 15 ml of mixture of equal volumes of *methyl alcohol* and *water* for thirty minutes and dilute to 25 ml with the same solvent mixture. Filter through a suitable membrane filter disc having an average pore diameter not greater than 0.8 µm, rejecting the first few ml of the filtrate, and transfer 1.0 ml to a 10-ml graduated flask. Add 3 ml of a 0.1 per cent w/v solution of *ascorbic acid* in *methyl alcohol*, 0.2 ml of a 0.009 M solution of hydrogen peroxide [prepared by accurately diluting *hydrogen peroxide solution (30 per cent)* that has been standardised by the titration with *0.1 N potassium permanganate*], mix, and dilute to volume with *hydrochloric acid*. After exactly thirty minutes, measure the *fluorescence* of the solution, using an

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

excitation wavelength of about 400 nm and an emission wavelength of about 570 nm and setting the spectrophotofluorimeter to zero with *water*, Appendix 5.15 C. Calculate the content of digitoxin, $C_{41}H_{64}O_{13}$, from the *fluorescence* obtained by carrying out the operation at the same time using a 0.0004 per cent w/v solution of *digitoxin R.S.* in a mixture of equal volumes of *methyl alcohol* and *water* and beginning at the words "transfer 1.0 ml ... .".

Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 80 and 120 per cent of the average except that for one tablet the content may be between 75 and 125 per cent of the average.

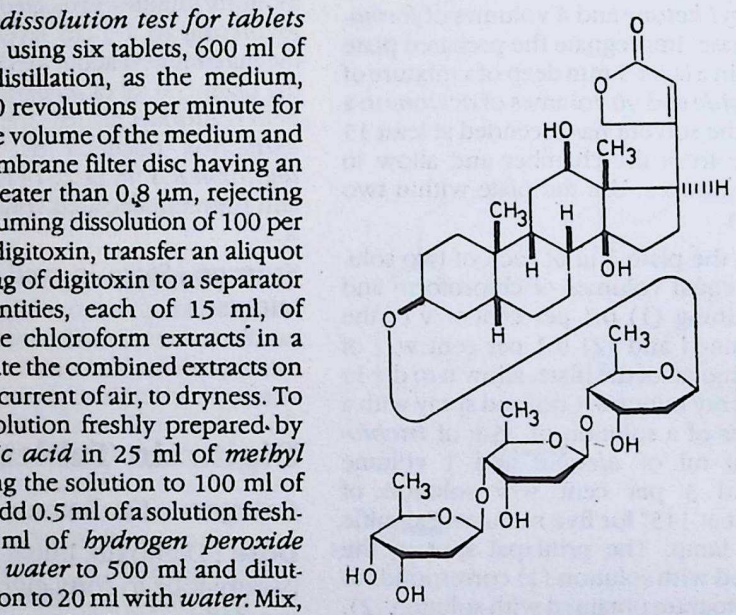
Dissolution : Carry out the *dissolution test for tablets and capsules*, Appendix 5.7, using six tablets, 600 ml of *water* freshly prepared by distillation, as the medium, and rotating the basket at 120 revolutions per minute for one hour. Withdraw a suitable volume of the medium and filter promptly through a membrane filter disc having an average pore diameter not greater than 0.8 µm, rejecting the first 1 ml of the filtrate. Assuming dissolution of 100 per cent of the stated amount of digitoxin, transfer an aliquot of the filtrate equivalent to 3 µg of digitoxin to a separator and extract with three quantities, each of 15 ml, of *chloroform* and combine the chloroform extracts in a glass-stoppered flask. Evaporate the combined extracts on a water-bath with the aid of a current of air, to dryness. To the residue add 5 ml of a solution freshly prepared by dissolving 35 mg of *ascorbic acid* in 25 ml of *methyl alcohol* and cautiously adding the solution to 100 ml of *hydrochloric acid*. Mix, and add 0.5 ml of a solution freshly prepared by diluting 1 ml of *hydrogen peroxide solution (30 per cent)* with *water* to 500 ml and diluting 1 ml of the resulting solution to 20 ml with *water*. Mix, and insert the stopper in the flask. After forty-five minutes, measure the *fluorescence* of the solution, Appendix 5.15 C, using an excitation wavelength of about 395 nm and an emission wavelength of about 575 nm and setting the spectrophotofluorimeter to zero with *water* and to 100, with a solution of suitable concentration prepared at the same time as the test solution, of *digitoxin R.S.* and treated in the same manner as the test-solution. The amount of digitoxin per tablet in the solution is not less than 75 per cent of the stated amount.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and finely powder 20 tablets. To a quantity of the powder equivalent to 1.25 mg of Digitoxin add 3.0 ml of *water*, swirl to disperse the powder and allow to stand for ten minutes with occasional swirling. Add 25.0 ml of *glacial acetic acid* and shake mechanically for one hour. Filter through a No. 1 Whatman paper, rejecting the first few ml of the filtrate. Pipette 4.0 ml into a 25-ml graduated flask, pipette 4.0 ml of *digitoxin standard solution* into a second 25-ml graduated flask, and 4.0 ml of a solution of 25 ml of *glacial acetic acid* and 3.0 ml of *water* into a third 25-ml graduated flask to serve as a reagent blank. Add 1.0 ml of *dimethyl sulphoxide* to each flask and dilute to 25 ml with *xanthydrol reagent*. Mix well and allow to stand in the dark for four and a half hours. Measure the *extinction* of the test and standard solutions at the maximum at about 550 nm, using the reagent blank in the reference cell, Appendix 5.15 A.

Storage : Store in well-closed, light-resistant containers.

Digoxin



$C_{41}H_{64}O_{14}$ Mol. Wt. 780.95

Category : Cardiotonic.

Dose : Initial dose, 1 to 1.5 mg; maintenance dose, 0.25 mg, once or twice daily. By intravenous injection, initial dose, 0.5 to 1 mg.

Description : Colourless crystals or white or almost white powder; odourless.

Solubility : Practically insoluble in *water*, in *chloroform* and in *solvent ether*; freely soluble in dilute *alcohol* and in *pyridine*.

Standards : Digoxin is 3β-[{O-2, 6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-O-2, 6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-2, 6-dideoxy-β-D-*ribo*-hexopyranosyl}oxy]-12β, 14-dihydroxy-5β-14β-card-20-(22)-enolide. It contains not less than 95.0 per cent and not more than the equivalent of 103.0 per cent of $C_{41}H_{64}O_{14}$, calculated with reference to the dried substance.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Identification : (A) Complies with **Identification** tests (A) and (B) described under Digitoxin.

(B) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *kieselghur G* as the coating substance and a mixture of 50 volumes of *xylene*, 50 volumes of *ethyl methyl ketone* and 4 volumes of *formamide* as the mobile phase. Impregnate the prepared plate by allowing it to stand in a layer 5-mm deep of a mixture of 10 volumes of *formamide* and 90 volumes of *acetone* in a closed chamber until the solvent has ascended at least 15 cm. Remove the plate from the chamber and allow it to stand for at least five minutes. Use the plate within two hours of impregnation. Apply separately to the plate 1 µl of each of three solutions in a mixture of equal volumes of *chloroform* and *methyl alcohol* containing (1) 0.5 per cent w/v of the solution being examined; (2) 0.5 per cent w/v of *digoxin R.S.*; and (3) 0.025 per cent w/v solution of *digitoxin R.S.* After removal of the plate, allow it to dry in an oven at 115° for twenty minutes. Cool and spray with a mixture of 15 volumes of a solution of 25 g of *trichloroacetic acid* in 100 ml of *alcohol* and 1 volume of a freshly prepared 3 per cent w/v solution of *chloramine T* and heat at 115° for five minutes. Examine under an ultra-violet lamp. The principal spot in the chromatogram obtained with solution (1) corresponds to the spot in the chromatogram obtained with solution (2) and any other spot in the chromatogram obtained with solution (1) is not more intense than the spot in the chromatogram obtained with solution (3).

Clarity and colour of solution : A 0.5 per cent w/v solution in a mixture of equal volumes of *chloroform* and *methyl alcohol* is clear and colourless.

Specific optical rotation : Between +13.6° and +14.2°, determined in 10 per cent w/v solution in *pyridine* and using mercury light at 546.1 nm, Appendix 5.12.

Gitoxin : Complies with the test described under Digitoxin.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 0.1 g by drying "in vacuo", Appendix 5.8.

Assay : Carry out the **Assay**, described under Digitoxin, using *digoxin R.S.* instead of *digitoxin R.S.*

Storage : Store in well-closed, light-resistant containers.

Digoxin Injection

Category : Cardiotonic.

Dose : Digoxin. By intramuscular or slow intravenous injection, 0.5 to 10 mg.

Usual strength : 1 mg in 4 ml.

Standards : Digoxin Injection is a sterile solution of Digoxin in Water for Injection and Alcohol or suitable solvents. It contains not less than 90.0 per cent w/v and not more than 110.0 per cent w/v of the stated amount of Digoxin, $C_{41}H_{64}O_{14}$.

Identification : Evaporate to dryness. The residue complies with **Identification** test (A) described under Digitoxin.

pH : Between 6.7 and 7.3, Appendix 5.10.

Other requirements : Complies with the requirements stated under Injection.

Assay : Protect the solution from light throughout the assay. Evaporate a quantity equivalent to 5 mg of Digoxin on a water-bath and dry at 105° for fifteen minutes. To the residue add 5 ml of a mixture of 65 volumes of *chloroform* and 35 volumes of *methyl alcohol* and dilute to 25.0 ml with *glacial acetic acid*. Dilute 10.0 ml of this solution to 30.0 ml with *glacial acetic acid* containing 0.005 per cent w/v of *ferric chloride* and 2 per cent v/v of *sulphuric acid* and allow to stand for one hour (solution A). Dissolve 10 mg of *digoxin R.S.* previously dried "in vacuo" for twenty-four hours, 30 mg of *citric acid*, and 72 mg of *anhydrous disodium hydrogen phosphate* in sufficient *glacial acetic acid* to produce 5 ml, add 10 ml of a mixture of 65 volumes of *chloroform* and 35 volumes of *methyl alcohol*, and dilute to 50.0 ml with *glacial acetic acid*. Dilute 10.0 ml of this solution to 30.0 ml with *glacial acetic acid* containing 0.005 per cent w/v of *ferric chloride* and 2 per cent v/v of *sulphuric acid* and allow to stand for one hour (solution B). Prepare a third solution by the method described for solution B, omitting the *digoxin R.S.* (solution C). Measure the *extinction* of a 1-cm layer of solutions A and B at the maximum at about 590 nm, Appendix 5.15 A, using solution C as the blank. Calculate the content of $C_{41}H_{64}O_{14}$ from the *extinction* of solution B and from the declared content of $C_{41}H_{64}O_{14}$ in *digoxin R.S.*

Storage : Store in single-dose, light-resistant containers.

Digoxin Tablets

Category : Cardiotonic.

Dose : Digoxin. Initial dose, 1 to 1.5 mg in single or divided doses; maintenance dose, 0.25 to 0.75 mg daily.

Usual strengths : 0.125 mg; 0.25 mg.

Standards : Digoxin Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Digoxin, $C_{41}H_{64}O_{14}$.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Identification : To a quantity of the powdered tablets equivalent to 0.25 mg of Digoxin, add 1 ml of *glacial acetic acid* containing 0.01 per cent w/v of *ferric chloride*, shake for a few minutes, filter through a sintered glass filter, and add to the filtrate 1 ml of *sulphuric acid* so as to form a subjacent layer; a pure brown ring free from red colour is formed at the junction of the liquids, and, after a short time, the acetic acid layer acquires an indigo colour.

Uniformity of content : For tablet containing the equivalent of 0.25 mg of Digoxin, place 1 tablet in 10 ml of *water* at 37°, agitate to disintegrate, add 56 ml of *alcohol*, shake for one hour, and add sufficient *alcohol (80 per cent)* to produce 100.0 ml. For tablets containing the equivalent of 0.125 mg of Digoxin, place one tablet in 5 ml of *water* at 37°, agitate to disintegrate, add 25 ml of *alcohol*, shake for one hour, and add sufficient *alcohol (80 per cent)* to produce 50.0 ml.

Filter the resulting solution through a suitable membrane filter disc having an average pore diameter not greater than 0.8 µm, rejecting the first few ml of the filtrate, and transfer 1.0 ml to a 10-ml graduated flask. Add 3 ml of a 0.1 per cent w/v solution of *L-ascorbic acid* in *methyl alcohol*, 0.2 ml of a 0.009 M solution of hydrogen peroxide [prepared by accurately diluting *hydrogen peroxide solution (30 per cent)* that has been standardised by titration with *0.5N potassium permanganate*], mix, and dilute to volume with *hydrochloric acid*. After exactly two hours, measure the *fluorescence* of the solution, Appendix 5.15 C, using an excitation wavelength of about 360 nm and an emission wavelength of about 490 nm and setting the spectrophotofluorimeter to zero with *water*. Calculate the content of digoxin, $C_{41}H_{64}O_{14}$, from the *fluorescence* obtained by carrying out the operation at the same time using a 0.00025 per cent w/v solution of *digoxin R.S.* in *alcohol (80 per cent)* and beginning at the words "transfer 1.0 ml.....".

Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The contents of each tablet is between 80 and 120 per cent of the average except that for one tablet the content may be between 75 and 125 per cent of the average.

Dissolution : Carry out the *dissolution test for tablets and capsules*, Appendix 5.7, using six tablets, 600 ml of *water* freshly prepared by distillation as the medium, and rotating the basket at 120 revolutions per minute for one hour. Filter the sample through a membrane filter disc having an average pore diameter not greater than 0.8 µm, rejecting the first 1 ml of the filtrate, and transfer 1.0 ml to a 10 ml graduated flask. Add 3 ml of a 0.1 per cent w/v solution of *L-ascorbic acid* in *methyl alcohol* and 0.2 ml of a 0.009 M solution of hydrogen peroxide [prepared by accurately diluting *hydrogen peroxide solution (30 per cent)* that has been standardised by titration with *0.1N potassium permanganate*], mix, and dilute to volume with *hydrochloric acid*. After exactly two hours measure the *fluorescence* of the solution, Appendix 5.15 C, using an excitation wavelength of about 360 nm and an emission wavelength of about 490 nm and setting the spectrophotofluorimeter to zero with *water* and to 100 with a solution prepared at the same time as the test solution as follows: Dilute 2.5 ml of a 0.100 per cent w/v solution of *digoxin R.S.* in *alcohol (80 per cent)* to 100 ml with *water*, dilute the resulting solution further with *water* to produce a solution containing in 1 ml an amount of digoxin equal to one-hundredth of the strength of the tablets being examined, transfer 1.0 ml of the solution to a 10-ml graduated flask and carry out the operation described above, beginning at the words "Add 3 ml.....". The amount of digoxin per tablet in solution is not less than 75 per cent of the prescribed or stated amount.

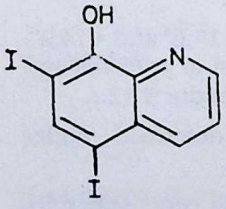
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and finely powder 25 tablets. Carry out the **Assay** described under Digitoxin Tablets and use 4.0 ml of *digoxin standard solution* in place of 4.0 ml of *digitoxin standard solution*.

Storage : Store in tightly-closed containers.

Di-iodohydroxyquinoline

Iodoquinol



$C_9H_5I_2NO$ Mol. Wt. 396.95

Category : Antiprotozoal.

Dose : 1 to 2 g daily.

Description : Light yellowish to yellowish-brown, micro-crystalline powder; odourless or with a faint odour; tasteless.

Solubility : Practically insoluble in *water*; sparingly soluble in *alcohol*, and in *solvent ether*.

Standards : Di-iodohydroxyquinoline is 5,7-di-iodoquinoline-8-ol. It contains not less than 97.0 per cent and not more than the equivalent of 100.5 per cent of $C_9H_5I_2NO$, calculated with reference to the dried substance.

Identification : (A) Heat a few crystals with about 1 ml of *sulphuric acid*; violet vapours of iodine are evolved.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

(B) Dissolve 10 mg in 100 ml of *dioxan* and dilute 5 ml to 100 ml with *ethyl alcohol*. The light absorption, in the range 230 to 330 nm, of a 1-cm layer of the resulting solution exhibits a maximum at 258 nm; *extinction* at 258, about 0.53, Appendix 5.15 A.

Free iodine and iodide : Shake 1 g with 20 ml of *water*, for thirty seconds, allow to stand for five minutes and filter. To 10 ml of the filtrate, add 1 ml of *dilute sulphuric acid* and 2 ml of *chloroform* and shake; the chloroform layer does not become violet. To the mixture add 5 ml of *dilute sulphuric acid* and 1 ml of *potassium dichromate solution* and shake for fifteen seconds, the chlorofom layer does not become deeper in colour than the colour produced in a control test made by diluting 2 ml of a solution containing 0.16 g of *potassium iodide* per litre of *water*, to 10 ml with *water*, adding 6 ml of *dilute sulphuric acid*, 1 ml of *potassium dichromate solution*, and 2 ml of *chloroform*, and shaking for fifteen seconds.

Sulphated ash : Not more than 0.2 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying "in vacuo" for four hours; Appendix 5.8.

Assay : Carry out the *oxygen-flask method for iodine*, Appendix 3.3.6, using 12 mg, accurately weighed, and a mixture of 10 ml of *water* and 2 ml of *N sodium hydroxide* as the absorbing liquid. Each ml of *0.02N sodium thiosulphate* is equivalent to 0.6616 mg of $C_9H_5I_2NO$.

Storage : Store in well-closed, light-resistant containers.

Di-iodohydroxyquinoline Tablets

Category : Anti-amoebic.

Dose : Di-iodohydroxyquinoline, 650 mg to 1.95 g daily, in divided doses, for not more than twenty days.

Usual strengths : 300 mg; 650 mg.

Standards : Di-iodohydroxyquinoline Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Di-iodohydroxyquinoline, $C_9H_5I_2NO$.

Identification : Heat a small quantity of the powdered tablets with 1 ml of *sulphuric acid*; violet vapours of iodine are evolved.

Disintegration : Maximum time, one hour, Appendix 5.6.1.

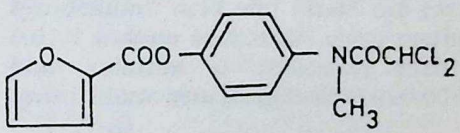
Soluble iodides : Digest a quantity of the powdered tablets, equivalent to 0.1 g of Di-iodohydroxyquinoline with 5 ml of *water* for ten minutes, cool, and filter. To the filtrate add 1 ml of *dilute hydrochloric acid*, two drops of *ferric chloride test-solution* and 2 ml of *chloroform*, shake gently and allow to separate; any violet colour in the chloroform is not more intense than that in a blank to which 1 ml of a 0.02 per cent w/v solution of *potassium iodide* has been added.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 12 mg of Di-iodohydroxyquinoline. Carry out the *oxygen-flask method*, Appendix 3.3.6, using a mixture of 10 ml of *water* and 2 ml of *N sodium hydroxide* as the absorbing liquid. When the process is complete add to the flask an excess (between 5 and 10 ml) of *acetic bromine solution* and allow to stand for two minutes. Remove the excess of bromine by the addition of *formic acid* (about 0.5 to 1 ml), rinse the sides of the flask with *water*, and sweep out any bromine vapour above the liquid with a current of air. Add 1 g of *potassium iodide* and titrate with *0.02N sodium thiosulphate*, using *starch solution* as indicator towards the end of the titration. Each ml of *0.02N sodium thiosulphate* is equivalent to 0.6616 mg of $C_9H_5I_2NO$.

Storage : Store in light-resistant containers.

Diloxanide Furoate



$C_{14}H_{11}Cl_2NO_4$ Mol. Wt. 328.15

Category : Anti-amoebic.

Dose : 1.5 g daily, in divided doses.

Description : White or almost white crystalline powder; odourless; tasteless.

Solubility : Very slightly soluble in *water*; soluble in *alcohol*, in *chloroform* and in *solvent ether*.

Standards : Diloxanide Furoate is 4-(*N*-methyl-2, 2-dichloroacetamido) phenyl-2-furoate. It contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of $C_{14}H_{11}Cl_2NO_4$, calculated with reference to the dried substance.

Identification : (A) Burn 20 mg by the *oxygen-flask method*, Appendix 3.3.6, using 10 ml of *N sodium hydroxide* as the absorbing liquid. When the process is complete, acidify the liquid with *nitric acid* and add *silver nitrate solution*; a white precipitate is produced.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

(B) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.0007 per cent w/v solution in *alcohol* exhibits a maximum only at 258 nm; *extinction* at 258 nm, about 0.49, Appendix 5.15A.

Melting range : Between 114° and 116°, Appendix 5.11.

Chloride : Shake 1 g with 40 ml of *water* for five minutes and filter; the filtrate complies with the *limit test for chlorides*, Appendix 3.2.2.

Furoic acid : Shake 3.0 g with 50 ml of *water*, filter and wash the residue with three quantities, each of 20 ml, of *water*. Titrate the combined filtrate and washings with *0.1N sodium hydroxide*, using *phenolphthalein solution* as indicator; not more than 1.3 ml is required.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.3 g, dissolve in 50 ml of *pyridine* and titrate with *0.1N tetrabutyl ammonium hydroxide*, protecting the solution from carbon dioxide of the atmosphere and determining the end-point potentiometrically using a glass electrode and a calomel electrode in which the saturated solution in *water* of *potassium chloride* is replaced by a saturated solution in *methyl alcohol* of *potassium chloride*. Perform a blank determination and make any necessary correction. Each ml of *0.1N tetrabutyl ammonium hydroxide* is equivalent to 0.03282 g of $C_{14}H_{11}Cl_2NO_4$.

Storage : Store in well-closed, light-resistant containers.

Diloxanide Furoate Tablets

Category : Anti-amoebic.

Dose : Diloxanide Furoate, 1.5 g daily, in divided doses, for ten days or more.

Usual strength : 500 mg.

Standards : Diloxanide Furoate Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Diloxanide Furoate, $C_{14}H_{11}Cl_2NO_4$.

Identification : The residue obtained in the **Assay** melts at about 115°, Appendix 5.11, and complies with **Identification** test (A) described under Diloxanide Furoate.

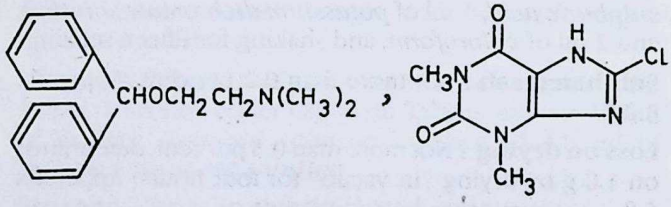
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 40 mg of Diloxanide Furoate and shake with 150 ml of *alcohol* for thirty minutes, add sufficient *alcohol* to produce 200.0 ml, mix and filter. Dilute 10.0 ml of the filtrate to 25.0 ml with *alcohol* and measure the *extinction* of the resulting solution at the maximum at about 258 nm, Appendix 5.15 A. Calculate the content of $C_{14}H_{11}Cl_2NO_4$ taking 705 as the value of E(1 per cent, 1-cm) at the maximum at about 258 nm.

Storage : Store in light-resistant containers.

Dimenhydrinate

Diphenhydramine Theoclate



$C_{17}H_{21}NO,C_7H_7ClN_4O_2$ Mol. Wt. 469.97

Category : Anti-emetic.

Dose : 25 to 100 mg.

Description : White, crystalline powder; odourless; taste, bitter and followed by local numbness.

Solubility : Sparingly soluble in *water*; freely soluble in *alcohol* and in *chloroform*; sparingly soluble in *solvent ether*.

Standards : Dimenhydrinate is the diphenhydramine salt of 8-chlorotheophylline. It contains not less than 53.0 per cent and not more than 55.5 per cent of diphenhydramine, $C_{17}H_{21}NO$, and not less than 44.0 per cent and not more than 47.0 per cent of 8-chlorotheophylline, $C_7H_7ClN_4O_2$, calculated with reference to the dried substance.

Identification : (A) Dissolve 0.25 g in 15 ml of *alcohol (50 per cent)*, add 15 ml of *water* and 2 ml of *dilute ammonia solution*, and extract with two quantities, each of 10 ml, of *solvent ether*, combine the extracts, wash with 5 ml of *water*, add 1 ml of *hydrochloric acid* and evaporate almost to dryness on a water-bath; the residue complies with **Identification** tests (A) and (B) described under Diphenhydramine Hydrochloride.

(B) Dissolve 0.25 g in 15 ml of *alcohol (50 per cent)*, add 15 ml of *water* and 2 ml of *dilute sulphuric acid* and cool for thirty minutes, scratch the tube to induce crystallisation; a precipitate is formed which, after washing with water and drying, melts at about 300° with decomposition, Appendix 5.11.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

(C) Dissolve 10 mg of the residue obtained in **Identification** test (B) in 1 ml of *hydrochloric acid*, add 0.1 g of *potassium chlorate*, and evaporate to dryness on a water-bath, a reddish residue remains which becomes purple when exposed to the vapour of *dilute ammonia solution*.

Melting range : Between 102° and 107°, Appendix 5.11.

Chloride : Precipitate silver chlorotheophyllinate from 0.8 g by the method described under **Assay** *for 8-chlorotheophylline*. Filter off the precipitate and acidify the filtrate with *nitric acid*; the solution remains clear or is only slightly opalescent.

Bromide and iodide : Mix 0.1 g in a test-tube with 50 mg of *sodium nitrite* and 10 ml of *chloroform*. Add 10 ml of *dilute hydrochloric acid*, stopper the tube and shake; the chloroform remains colourless.

Foreign substances : Complies with the test described under Diphenhydramine Hydrochloride.

Sulphated ash : Not more than 0.2 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying 'in vacuo' for twenty-four hours, Appendix 5.8.

Assay : *For diphenhydramine* — Weigh accurately about 0.15 g and dissolve in 75 ml of *glacial acetic acid*; titrate with *0.05N perchloric acid*, determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.05N perchloric acid* is equivalent to 0.01277 g of diphenhydramine, $C_{17}H_{21}NO$.

For 8-chlorotheophylline — Weigh accurately about 0.8 g, add 50 ml of *water*, 3 ml of *dilute ammonia solution* and 5 ml of a 10 per cent w/v solution of *ammonium nitrate*, warm on a water-bath for five minutes, add 25.0 ml of *0.1N silver nitrate* and continue warming for a further fifteen minutes, shaking frequently. Cool, dilute to 200 ml with *water*, and allow to stand for sixteen hours; filter, wash the residue with *water*, neutralise the combined filtrate and washings to *litmus paper* with *nitric acid*, add 2 ml in excess, and titrate the excess of silver nitrate with *0.1N ammonium thiocyanate*, using *ferric ammonium sulphate solution* as indicator. Each ml of *0.1N silver nitrate* is equivalent to 0.02146 g of $C_7H_7ClN_4O_2$.

Storage : Store in well-closed, light-resistant containers.

Dimenhydrinate Tablets

Category : Antihistaminic (antinauseant).

Dose : Dimenhydrinate, 25 to 100 mg.

Usual strength : 50 mg.

Standards : Dimenhydrinate Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Dimenhydrinate, $C_{17}H_{21}NO, C_7H_7ClN_4O_2$.

Identification : Triturate a quantity of the powdered tablets equivalent to 0.5 g of Dimenhydrinate with 25 ml of warm *alcohol* and filter. Dilute the filtrate with 40 ml of *water* and again filter; the filtrate complies with **Identification** tests (A) to (C) described under Dimenhydrinate.

Foreign substances : Comply with the test described under Dimenhydrinate, applying to the plate 5 µl of each of the following solutions. For solution (1) shake a quantity of the powdered tablets equivalent to 0.1 g of Dimenhydrinate with three quantities, each of 10 ml, of *chloroform*, filter, and evaporate the combined filtrate almost to dryness; dissolve the residue in 5 ml of *chloroform*. For solution (2) dilute 1 volume of solution (1) to 100 volumes with *chloroform*.

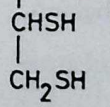
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh 20 tablets and reduce to a fine powder. Weigh accurately a quantity of the powder equivalent to about 0.1 g of Dimenhydrinate and dissolve as completely as possible in 20 ml of *water*, add 10 ml of *5N ammonia*, mix, extract successively with 15, 15, 15, 10 and 10 ml of *solvent ether*, and wash the combined extracts with 10 ml of *water*. Remove the ether, warm the residue with 10 ml of *alcohol* until dissolved, cool, add 50.0 ml of *0.01N hydrochloric acid* and titrate the excess of acid with *0.01N sodium hydroxide*, using *methyl red-methylene blue solution* as indicator. Each ml of *0.01N hydrochloric acid* is equivalent to 0.0047 g of $C_{17}H_{21}NO$, $C_7H_7ClN_4O_2$.

Storage : Store in well-closed containers.

Dimercaprol

B.A.L.



$C_3H_8OS_2$ Mol. Wt. 124.22

Category : Antidote in heavy metals poisoning, metal complexing agent.

Dose : By intramuscular injection, 2 to 3 mg per kg

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

of body weight every four hours during the first day, and subsequently in accordance with the needs of the patient.

Description : Clear, colourless or almost colourless liquid; odour, strong, characteristic and alliaceous.

Solubility : Soluble in *water*, in *alcohol*, in *methyl alcohol* and in *benzyl benzoate*.

Standards : Dimercaprol is 2, 3-dimercaptopropanol. It contains not less than 98.5 per cent w/w and not more than the equivalent of 101.5 per cent w/w of $C_3H_8OS_2$.

Identification : (A) Dissolve 0.1 ml in 4 ml of *water* and to 2 ml of the solution add *lead acetate solution*. A yellow precipitate is obtained.

(B) To 2 ml of the solution prepared for **Identification** test A add 1 ml of *0.1N iodine*. The colour of iodine is immediately discharged.

pH : Between 5.0 and 6.5, determined in a saturated solution, Appendix 5.10.

Wt. per ml : Between 1.238 g and 1.240 g, Appendix 5.19.

Refractive index : Between 1.568 and 1.574, determined at 20°, Appendix 5.14.

Iron : Ignite 2 g with 1 g of *anhydrous sodium carbonate*, cool, dissolve the residue in 15 ml of *dilute hydrochloric acid*, and dilute to 45 ml with *water*; the solution complies with the *limit test for iron*, Appendix 3.2.5.

Halide : To 2.0 g add 25 ml of *0.5N alcoholic potassium hydroxide* and heat under reflux condenser for two hours. Remove the alcohol by evaporation in a current of warm air, add 20 ml of *water* and cool. Add a mixture of 10 ml of *strong hydrogen peroxide solution* and 40 ml of *water*. Boil gently for 10 minutes; cool and filter rapidly. Add 10 ml of *dilute nitric acid* and 5.0 ml of *0.1N silver nitrate* and titrate the excess of silver nitrate with *0.1N ammonium thiocyanate*, using *ferric ammonium sulphate solution* as indicator. Repeat the operation without the dimercaprol. The difference in the volumes of *0.1N ammonium thiocyanate* used in two titrations is not more than 1.0 ml.

Stability : Loses not more than 5.0 per cent of its content of $C_3H_8OS_2$ (as determined in the **Assay** given below), when heated at 140° for two hours.

Assay : Weigh accurately about 0.1 g from a sample through which *oxygen-free nitrogen* has been passed for about 10 minutes, add 20 ml of *0.1N hydrochloric acid* and titrate immediately with *0.1N iodine*. Each ml of *0.1N iodine* is equivalent to 0.00621 g of $C_3H_8OS_2$.

Storage : Store in well-closed, light-resistant containers, at a temperature not exceeding 5°.

Dimercaprol Injection

B.A.L. Injection

Category : Antidote in heavy metal poisoning, metal complexing agent.

Dose : By intramuscular injection 0.02 to 0.03 ml per kg of body weight every four hours during the first day, and subsequently in accordance with the needs of the patient.

Usual strength : 50 mg per ml.

Description : Clear yellow, viscous solution, having a pungent, disagreeable odour.

Standards : Dimercaprol Injection is a sterile solution of Dimercaprol in a mixture of Benzyl Benzoate and Arachis Oil. It contains not less than 90.0 per cent w/v and not more than 110.0 per cent w/v of the stated amount of $C_3H_8OS_2$.

Reaction : Shake with an equal volume of *water* for two minutes and set aside for separation; pH of the aqueous layer after filtration through a neutral filter is between 5.5 and 6.5, Appendix 5.10.

Refractive index : Between 1.481 and 1.483, determined at 20°, Appendix 5.14.

Wt. per ml : About 0.978 g, Appendix 5.19.

Other requirements : Complies with the requirements stated under Injections.

Assay : Weigh accurately about 2.0 g in a tared Erlenmeyer flask of 150 ml capacity. Add 100 ml of a mixture of one volume of *chloroform* and 3 volumes of *methyl alcohol*, shake to dissolve, and titrate with *0.1N iodine* to a permanent yellow colour. Perform a blank determination and make any necessary correction. Each ml of *0.1N iodine* is equivalent to 0.006211 g of $C_3H_8OS_2$. Determine the *weight per ml* of the injection, Appendix 5.19 and calculate the percentage w/v of dimercaprol, $C_3H_8OS_2$.

Storage : Store in single-dose or multi-dose light-resistant containers.

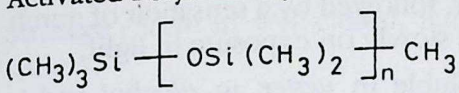
Labelling : The label on the container states (1) the nature of the solvent; (2) "For intramuscular injection only".

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Activated Dimethicone

Activated Polydimethylsiloxane; Simethicone



Category : Defoaming agent.

Dose : 40 to 100 mg, four times daily.

Description : Translucent, grey, viscous liquid; almost odourless; tasteless.

Solubility : Insoluble in *water* and in *alcohol*; the liquid phase is soluble in *chloroform*, in *solvent ether* and in *benzene*, but silicon dioxide remains as a residue in the solvent.

Standards : Activated Dimethicone is a mixture of polymethylsiloxane containing repeating units of the formula $[-(CH_3)_2SiO-]_n$ stabilised with trimethylsiloxy end-blocking units of the formula $[-(CH_3)_3SiO-]$ and finely-divided silicon dioxide. It contains not less than 90.0 per cent of polydimethylsiloxane ($[-(CH_3)_2SiO-]_n$).

Identification : (A) To 50 mg add 25 ml of *carbon tetrachloride* and swirl to disperse. Add 50 ml of *dilute hydrochloric acid* and shake for five minutes. Transfer to a separator and remove about 5 ml of the lower layer to a stoppered tube containing 0.5 g of *anhydrous sodium sulphate*. Shake vigorously and centrifuge the mixture until a clear supernatant liquid is obtained. The *infra-red absorption spectrum* of the resulting solution exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of a solution of *polydimethylsiloxane R.S.*, Appendix 5.15B.

(B) Centrifuge 1 g until an almost clear liquid separates and a white residue is obtained. Transfer the residue to a platinum crucible, add 0.2 g of *anhydrous potassium carbonate* and ignite at a red heat and cool. Dissolve the residue in 2 ml of freshly-distilled *water*, warm and slowly add 2 ml of *ammonium molybdate solution*; a deep yellow colour is produced.

Viscosity : Not less than 300 centistokes, Appendix 5.18, determined in the liquid obtained in the following manner. Mix 3 parts by weight of the substance being examined with 7 parts by weight of *n-hexane* and centrifuge until an almost clear supernatant liquid is obtained. Decant the supernatant liquid into a shallow container, and allow the hexane to evaporate. Heat at 70° for thirty minutes, and allow to cool.

Heavy metals : Not more than 10 parts per million, determined on 2.0 g by Method B, Appendix 3.2.4.

Defoaming activity : Prepare a test solution by transferring 0.2 g to a 100-ml bottle, add 50 ml of *t-butyl alcohol* and shake vigorously, warming, if necessary to effect solution. Add dropwise, 0.5 ml of this solution to a clean, unused, cylindrical 250-ml glass jar, fitted with a 50 mm cap, containing 100 ml of a 1.0 per cent w/v solution of *octoxynol*. Cap the jar and shake for 10 seconds vigorously. Record the time required in seconds for the foam to collapse. The time for foam collapse is determined at the instant the first portion of foam-free liquid surface appears, measured from the end of the shaking period. The defoaming activity time is not more than 15 seconds.

Assay : Weigh accurately about 50 mg, transfer to a narrow-mouthed glass bottle and add 25.0 ml of *carbon tetrachloride*. Swirl to disperse, add 50 ml of *dilute hydrochloric acid*, close the bottle securely with a cap having an inert liner, and shake for exactly five minutes. Transfer the mixture to a 125-ml separator, and remove about 5 ml of the lower layer to a stoppered test-tube containing 0.5 g of *anhydrous sodium sulphate*. Close the test-tube, agitate vigorously, and centrifuge the mixture until a clear supernatant liquid is obtained. Prepare a blank by mixing 10 ml of *carbon tetrachloride* with 0.5 g of *anhydrous sodium sulphate* and centrifuging to obtain a clear supernatant liquid. Determine the *extinction* of a 0.5 ml layer of the solution at the maximum at about 7.9 µm with a suitable infra-red spectro-photometer, Appendix 5.15B, using the blank to set the instrument. Calculate the content of $[-(CH_3)_2SiO-]_n$ from the *extinction* obtained by repeating the assay on a 0.2 per cent w/v solution of *polydimethylsiloxane R.S.* in place of the substance being examined and from the declared content of $[-(CH_3)_2SiO-]_n$ in the *polydimethylsiloxane R.S.*

Storage : Store in tightly-closed containers.

Diodone Injection

Category : Radio-opaque medium used in urography and angiography.

Dose : The dose is decided in accordance with the diagnostic procedure undertaken.

Description : Clear, almost colourless to pale-yellow liquid.

Usual strengths : 35 per cent; 50 per cent; 70 per cent w/v.

Standards : Diodone Injection is a sterile aqueous solution of the diethanolamine salt of 3, 5-di-iodo-4-pyridone-*N*-acetic acid. It contains a quantity of iodine, I, equivalent to not less than 48.0 per cent and not more than 52.0 per cent w/v of the stated amount of Diodone. It may contain a suitable stabilising agent.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Identification : (A) Dilute 10 ml with 10 ml of *water*, add a slight excess of *dilute hydrochloric acid*, filter, and wash the residue with *water*, reserving the combined filtrate and washings; the residue after drying at 105° melts at about 245°, Appendix 5.11.

(B) Dilute the combined filtrate and washings from the previous test to 100 ml, cool in ice-water, filter and evaporate to a syrupy consistency. Add 5 ml of *ethyl alcohol*, neutralise with *N sodium hydroxide*, using *litmus paper* as indicator; filter and dilute to 10 ml with *ethyl alcohol*. Add 1 g of *picric acid*, heat to boiling and finally cool in ice-water. Collect the residue on a filter paper, recrystallise from *alcohol* and dry "in vacuo"; the residue melts at about 110°, Appendix 5.11.

pH : Between 7.0 and 8.0, Appendix 5.10.

Wt. per ml : 1.18 to 1.20 g (for 35 per cent solution); 1.26 to 1.28 g (for 50 per cent solution); 1.355 to 1.390 g (for 70 per cent solution) determined at 30°, Appendix 5.19.

Inorganic iodides : Take 10 ml of the filtrate from **Identification** test (A), add 1 ml of *chloroform* and 2 drops of *ferric chloride test-solution* and shake; no colouration appears in the chloroform layer.

Sulphated ash : Not more than 0.1 per cent w/v, Appendix 3.2.7.

Other requirements : Complies with the requirements stated under Injections.

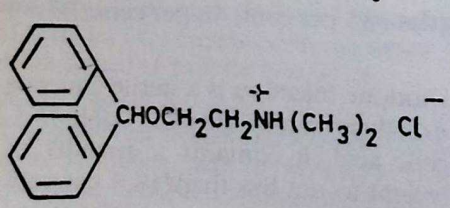
Assay : Carry out the *oxygen-flask method for iodine*, Appendix 3.3.6, using a quantity equivalent to 20 mg of the diethanolamine salt. Determine the *weight per ml* of the sample and calculate the percentage w/v of Iodine, I.

Storage : Store in light-resistant containers. Solid matter may separate on standing. This should be redissolved by warming before use.

Labelling : The label on the container states the strength as the percentage w/v of diodone.

NOTE—Care should be taken to avoid contact of the solution with metal.

Diphenhydramine Hydrochloride



$C_{17}H_{21}NO, HCl$ Mol. Wt. 291.82

Category : Antihistaminic.

Dose : 50 to 200 mg daily, in divided doses.

Description : White, crystalline powder; odourless; taste, bitter, followed by a sensation of numbness. It darkens slowly on exposure to light.

Solubility : Soluble in *water*, in *alcohol* and in *chloroform*; sparingly soluble in *acetone*; very slightly soluble in *solvent ether*.

Standards : Diphenhydramine Hydrochloride is 2-benzhydryloxyethyl-*N*,*N*-dimethylammonium chloride. It contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of $C_{17}H_{21}NO, HCl$, calculated with reference to the dried substance.

Identification : (A) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.025 per cent w/v solution in *alcohol* exhibits three maxima, at 253 nm, 258 nm and 264 nm; *extinction* at 253 nm, about 0.31 at 258 nm, about 0.38 and at 264 nm, about 0.3, Appendix 5.15 A.

(B) To 10 ml of a hot 1 per cent w/v solution, add dropwise *picric acid solution* until precipitation is complete; the precipitate, after recrystallisation from *alcohol* melts at about 130°, Appendix 5.11.

(C) Dissolve 0.1 g in 10 ml of *water* and add *ammonium reinackate solution*; a pink precipitate is produced.

(D) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

Melting range : Between 168° and 172°, Appendix 5.11.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel H* as the coating substance and a mixture of 80 volumes of *chloroform*, 20 volumes of *methyl alcohol* and 1 volume of *diethylamine* as the mobile phase. Apply separately to the plate 5 µl of each of two freshly prepared solutions in *methyl alcohol* containing (1) 2.0 per cent w/v of the substance being examined and (2) 0.02 per cent of the substance being examined. After removal of the plate, allow it to dry in air for five minutes; spray with a 20 per cent v/v solution of *sulphuric acid* in *alcohol* and heat at 120° for about ten minutes until the spots appear. Any spot in the chromatogram obtained with solution (1), other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (2).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.75 g and dissolve in 40 ml of *glacial acetic acid*, add 10 ml of *mercuric acetate solution* and titrate with *0.1N perchloric acid*, using *crystal-violet solution* as indicator. Perform a blank

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

determination and make any necessary correction. Each ml of *0.1 perchloric acid* is equivalent to 0.02918 g of $C_{17}H_{21}NO,HCl$.

Storage : Store in well-closed, light-resistant containers.

Diphenhydramine Capsules

Diphenhydramine Hydrochloride Capsules

Category : Antihistaminic.

Dose : Diphenhydramine Hydrochloride, 50 to 200 mg daily, in divided doses.

Usual strengths : 25 mg; 50 mg.

Standards : Diphenhydramine Capsules contain not less than 93.0 per cent and not more than 107.0 per cent of the stated amount of Diphenhydramine Hydrochloride, $C_{17}H_{21}NO,HCl$.

Identification : Extract a quantity of the contents of the capsules equivalent to 0.1 g of Diphenhydramine Hydrochloride with two quantities, each of 15 ml, of *chloroform*. Evaporate the combined extracts to dryness on a water-bath and dry the residue at 80° for one hour; the residue melts at about 168°, Appendix 5.11, and complies with **Identification** tests (B), (C) and (D) described under Diphenhydramine Hydrochloride.

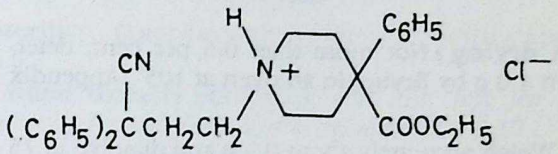
Related substances : Comply with the test described under Diphenhydramine Hydrochloride, applying to the plate 5 µl of each of the following solutions. For solution (1) shake a quantity of the contents of the capsules equivalent to 50 mg of Diphenhydramine Hydrochloride with three quantities, each of 10 ml, of *chloroform*, filter, and evaporate the combined filtrate almost to dryness; dissolve the residue in 5 ml of *chloroform*. For solution (2) dilute 1 volume of solution (1) to 100 volumes with *chloroform*.

Other requirements : Comply with the requirements stated under Capsules.

Assay : Weigh accurately a quantity of a mixed contents of 20 capsules and transfer to a 100-ml volumetric flask, add sufficient *water* to produce 100.0 ml, shake well to dissolve and filter. To a volume of the filtrate equivalent to 0.3 g of Diphenhydramine Hydrochloride add 5 g of *sodium chloride* and 5 ml of *sodium hydroxide solution*, and extract with successive quantities, each of 20 ml, of *solvent ether* until complete extraction is effected. Wash the combined extracts, with two quantities, each of 5 ml, of *water*, extract the combined washings with two quantities, each of 10 ml of *solvent ether*, add the ether to the combined ether extracts and evaporate to about 10 ml. Add 15.0 ml of *0.1N hydrochloric acid*, warm gently to complete the removal of the ether, cool and titrate the excess of acid with *0.1N sodium hydroxide* using *methyl red solution* as indicator. Each ml of *0.1N hydrochloric acid* is equivalent to 0.02918 g of $C_{17}H_{21}NO,HCl$.

Storage : Store in tightly-closed containers.

Diphenoxylate Hydrochloride



$C_{30}H_{32}N_2O_2,HCl$ Mol. Wt. 489.06

Category : Antidiarrhoeal.

Dose : 5 to 30 mg daily, in divided doses.

Description : White or almost white crystalline powder; odourless.

Solubility : Slightly soluble in *water*; freely soluble in *chloroform*; soluble in *methyl alcohol*; sparingly soluble in *alcohol* and in *acetone*; practically insoluble in *solvent ether*.

Standards : Diphenoxylate Hydrochloride is the 1-(3-cyano-3, 3-diphenylpropyl)-4-ethoxycarbonyl-4-phenylpiperidinium chloride. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_{30}H_{32}N_2O_2,HCl$, calculated with reference to the dried substance.

Identification : (A) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.05 per cent w/v solution in a mixture of 1 volume of *N hydrochloric acid* and 99 volumes of *methyl alcohol* exhibits three maxima, at 252 nm, 258 nm and 264 nm; *extinction* at 252 nm, about 0.6, at 258 nm, about 0.65 and at 264 nm, about 0.5, Appendix 5.15 A.

(B) To 5 ml of a 0.1 per cent w/v solution add 0.1 ml of *potassium mercuri-iodide solution*; a cream coloured precipitate is produced.

(C) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

Melting range : Between 220° and 226°, Appendix 5.11.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using a slurry of *silica gel G* and *0.5N sodium hydroxide* as the coating substance, and a mixture of equal volumes of *chloroform* and *n-hexane* as the mobile phase. Apply separately to the plate 3 µl of each of the following solutions in *chloroform* containing (1) 10.0 per cent w/v of the substance being examined, (2) 0.1 per cent w/v of *1-bromo-3-cyano-3, 3-*

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

diphenylpropane R.S. and (3) 0.1 per cent w/v of *4-cyano-4-phenyl-1-tolysulphonylpiperidine R.S.* After removal of the plate allow it to dry in air and spray with a 0.5 per cent w/v solution of *iodine* in *chloroform*. Repeat the spraying if necessary and examine immediately. Any spots in the chromatogram obtained with solution (1), other than the principal spot, are not more intense than the proximate spots in the chromatograms obtained with solutions (2) and (3).

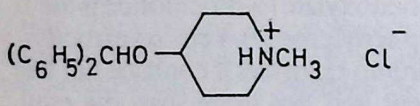
Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.6 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.3 g and dissolve in 75 ml of *glacial acetic acid*. Add 4 ml of *mercuric acetate solution* and titrate with *0.1N perchloric acid*, determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.04891 g of $C_{30}H_{32}N_2O_2$, HCl.

Storage : Store in well-closed containers.

Diphenylpyraline Hydrochloride



$C_{19}H_{23}NO$, HCl Mol. Wt. 317.86

Category : Antihistaminic.

Dose : 5 to 20 mg daily, in divided doses.

Description : White or almost white powder; odourless or almost odourless.

Solubility : Very soluble in *water*, freely soluble in *alcohol* and in *chloroform*; insoluble in *solvent-ether*.

Standards : Diphenylpyraline Hydrochloride is 4-benzhydryloxy-1-methyl-piperidinium chloride. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_{19}H_{23}NO$, HCl, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *diphenylpyraline hydrochloride R.S.*, Appendix 5.15 B.

(B) Dissolve 10 mg in 10 ml of *sulphuric acid*; an orange solution is produced. To 5 ml of the solution add 0.2 ml of *potassium dichromate solution*, warm, and allow to stand; the colour of the solution slowly changes from red to brown. Pour the remainder of the solution into about 10 ml of *water*; a colourless, opalescent solution is produced.

(C) To 10 ml of a hot 1 per cent w/v solution add dropwise *picric acid solution* until precipitation is complete; the precipitate after recrystallising from *alcohol*, melts at about 168°, Appendix 5.11.

(D) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

Melting range : Between 204° and 209°, Appendix 5.11.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.6 g and dissolve in 80 ml of *glacial acetic acid*. Add 10 ml of *mercuric acetate solution* and titrate with *0.1N perchloric acid*, using *crystal-violet solution* as indicator. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.03179 g of $C_{19}H_{23}NO$, HCl.

Storage : Store in tightly-closed, light-resistant containers.

Diphtheria Antitoxin

Category : Immunising agent.

Dose : By subcutaneous or intramuscular injection, prophylactic, 500 to 2000 International Units; therapeutic, not less than 10,000 International Units.

Description : Almost colourless or very faintly yellow to slightly opalescent liquid.

Standards : Diphtheria Antitoxin is a sterile preparation containing the specific antitoxic globulins or their derivatives obtained by purification from native serum or plasma of healthy horses or other suitable animals and having the specific power of neutralising the toxin formed by *Corynebacterium diphtheriae*. It has a potency of not less than 1000 International Units per ml in the case of antitoxin obtained from horse serum and not less than 500 International Units per ml for antitoxin obtained from other animals. It may contain a suitable preservative.

Identification : It specifically neutralises and renders the toxins formed by *Corynebacterium diphtheriae* harmless to susceptible animals.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Other requirements : Complies with the requirements for general tests stated under Antisera.

Potency : Carry out the *determination of potency of diphtheria antitoxin*, Appendix 2.14.

Storage : Store in containers protected from light, at a temperature between 2° and 8°. It should not be allowed to freeze.

Labelling : The label on the container states (1) the number of Units per ml; (2) the species of animals from which the preparation has been made; (3) the recommended dose; (4) the storage conditions; (5) the date after which it is not intended to be used.

Diphtheria and Tetanus Vaccine (Adsorbed)

Diphtheria and Tetanus Toxoid (Adsorbed)

Category : Active immunising agent.

Dose : By deep intramuscular injection, two injections of 0.5 ml, four to six weeks apart, and a third, reinforcing dose of 0.5 ml, six to eight months later.

Standards : Diphtheria and Tetanus Vaccine (Adsorbed) is a sterile suspension of purified diphtheria vaccine and purified tetanus vaccine adsorbed on a mineral carrier such as aluminium hydroxide or aluminium phosphate. The formaldehyde treated toxoids are prepared from the toxins produced by the growth in suitable media of *Corynebacterium diphtheriae* and *Clostridium tetani*, by methods that avoid reversibility of the toxoids.

The vaccine is prepared by mixing purified diphtheria toxoid containing not less than 1500 flocculation equivalents (1500 Lf) and purified tetanus toxoid containing not less than 1000 flocculation equivalents (1000 Lf) per mg of protein nitrogen, with a suspension of aluminium hydroxide or aluminium phosphate in a 0.9 per cent w/v solution of Sodium Chloride or other appropriate solution isotonic with blood. The final vaccine contains a suitable preservative other than any of the phenol or cresol groups.

It contains not less than 15 Lf of diphtheria toxoid and not less than 5 Lf of tetanus toxoid per dose of 0.5 ml.

Description : White, turbid liquid; the mineral carrier may tend to settle down slowly on keeping.

Identification : When injected into suitable laboratory animals, it induces diphtheria antitoxin and tetanus antitoxin in the circulating blood of the animals.

pH : Between 6.5 and 7.0, Appendix 5.10.

Aluminium : Not more than 1.25 mg of Al per dose stated on the label, Appendix 3.3.1.

Free formaldehyde : Complies with the *test for free formaldehyde*, Appendix 3.2.3.

Thiomersal (if present) : Between 0.005 per cent and 0.02 per cent w/v, Appendix 4.7.

Sterility : Complies with the *tests for sterility*, Appendix 4.6.

Undue toxicity : Complies with the *test for undue toxicity for vaccines and sera*, Appendix 2.37.

Specific toxicity : Use not fewer than five normal healthy guinea-pigs weighing between 250 and 350 g, which have been maintained for at least one week on a uniform, unrestricted diet and have not lost weight during the period and which have not previously been treated with any material that will interfere with the test. Weigh the animals separately and record the weight. Inject subcutaneously five times the dose stated on the label into each of the animals. Weigh all the animals at weekly intervals and on the thirtieth day. None of the animals shall die or show signs of diphtheria or tetanus toxaemia within 30 days or lose weight at the end of the test. If more than one animal die in the second test, the vaccine fails the test.

Potency : (a) *For diphtheria toxoid*—Determine by either of the following two methods:

(1) Inject subcutaneously on each of two occasions separated by an interval of not more than four weeks, one-fiftieth of the stated human dose diluted to 1 ml with *saline solution*, into each of ten normal, healthy guinea-pigs weighing between 250 and 350 g. Not earlier than two weeks and not later than three weeks after the second injection, collect the serum from each animal and determine the antitoxin content of the serum of each animal. The geometric mean of the antitoxin contents shall be not less than 2 I.U. per ml with reference to the *Diphtheria Antitoxin Standard*.

(2) Carry out the *biological assay of adsorbed diphtheria vaccine*, Appendix 2.21.

(b) *For tetanus toxoid*—Complies with the test for **Potency** described under Tetanus Vaccine (Adsorbed).

Storage : Store in single-dose or multiple-dose containers at a temperature between 2° and 8°. The vaccine should not be frozen.

Labelling : The label on the container states (1) the human dose; (2) the name of the mineral carrier; (3) the name and proportion of any added preservative; (4) the words "Not to be frozen"; (5) the date after which it is not intended to be used; (6) the storage conditions.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Diphtheria, Tetanus and Pertussis Vaccine (Adsorbed)

Diphtheria and Tetanus Toxoid and Pertussis Vaccine (Adsorbed)

Category : Active immunising agent.

Dose : By intramuscular injection, three injections of 0.5 ml, four to six weeks apart, and a fourth, reinforcing dose of 0.5 ml, six to eight months later.

Standards : Diphtheria, Tetanus and Pertussis Vaccine (Adsorbed) is a sterile suspension prepared by adsorbing formaldehyde-treated diphtheria toxoid and tetanus toxoid on a mineral carrier such as aluminium hydroxide or aluminium phosphate and adding a suspension of killed *Bordetella pertussis*. The toxoids prepared from the toxins produced by the growth in suitable media of *Corynebacterium diphtheriae* and *Clostridium tetani* by methods which avoid reversibility of the toxoid. Diphtheria toxoid containing not less than 1500 flocculation equivalents (1500 Lf) and tetanus toxoid containing not less than 1000 flocculation equivalents (1000 Lf) per mg of protein nitrogen are added to a suspension of hydrated aluminium phosphate or aluminium hydroxide in a 0.9 per cent w/v solution of Sodium Chloride or in any other solution isotonic with blood and then mixed with a quantity of a suspension of killed *Bordetella pertussis* such that the final product contains not more than 20×10^9 bacilli in each human dose. The final vaccine contains a suitable preservative other than any of the phenol or cresol groups. It contains not less than 15 Lf of diphtheria toxoid and not less than 5 Lf of tetanus toxoid per dose of 0.5 ml.

Description : White turbid liquid; the mineral carrier may tend to settle down slowly on keeping.

Identification : (A) Complies with the **Identification** test described under Diphtheria and Tetanus Vaccine (Adsorbed).

(B) When injected into suitable laboratory animals, it confers an active immunity against pertussis.

pH : Between 6.7 and 7.3, Appendix 5.10.

Aluminium; Free formaldehyde; Undue toxicity : Complies with the tests described under Diphtheria and Tetanus Vaccine (Adsorbed).

Thiomersal (if present) : Between 0.005 per cent and 0.05 per cent w/v, Appendix 4.7.

Sterility : Complies with the *test for sterility*, Appendix 4.6.

Specific toxicity : (A) Complies with the test for **Specific toxicity** described under Tetanus Vaccine (Adsorbed).

(B) Use ten mice of the same sex, each weighing between 14 and 16 g; the mice should have free access to food and water at all times during the test. Note the individual weights of the mice immediately before the test. Inject intraperitoneally into each mouse a volume equivalent to 10×10^9 bacilli of *B. pertussis* and diluted to 0.5 ml with *saline solution* (control). The vaccine passes the test if at the end of seven days the average weight gain per mouse is not less than 50 per cent of the weight gain per mouse of the control group. In addition, none of the animals dies in this period. If one of the animals dies, repeat the test. The vaccine passes the test if the number of deaths does not exceed 5 per cent of the total number of animals used.

Potency : (a) *For diphtheria toxoid* – Complies with the test described under Diphtheria and Tetanus Vaccine (Adsorbed).

(b) *For tetanus toxoid* – Complies with the test described under Tetanus Vaccine (Adsorbed), but if the test is performed on mice, the lower fiducial limit of error of the estimated potency is not less than 60 Units per dose.

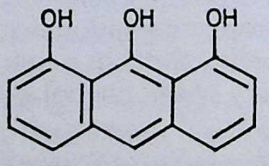
(c) *For pertussis vaccine* – Carry out the *biological assay of pertussis vaccine*, Appendix 2.22. The potency shall be not less than 4 Units per single human dose or 12 Units per total human immunising dose.

Storage : Store in single-dose or multiple-dose containers at a temperature between 2° and 8°. The vaccine should not be frozen.

Labelling : The label on the container states (1) the human dose; (2) the name of the mineral carrier; (3) the name and proportion of any added preservative; (4) the words "Not to be frozen"; (5) the date after which it is not intended to be used; (6) the storage conditions.

Dithranol

Dioxyanthranol, Anthralin



$C_{14}H_{10}O_3$ Mol. Wt. 226.23

Category : Topical antipsoriatic.

Description : Yellow to yellowish-brown powder; odourless; tasteless.

Solubility : Practically insoluble in *water*; slightly

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

soluble in *alcohol* and in *solvent ether*; soluble in *chloroform* and in *benzene*.

Standards : Dithranol is a mixture of 1, 8, 9-anthracenetriol and its tautomers. It contains not less than 95.0 per cent and not more than the equivalent of 100.5 per cent of $C_{14}H_{10}O_3$, calculated with reference to the dried substance.

Identification : Dissolve 5 mg in 5 ml of *N sodium hydroxide*; a clear fluorescent yellow or orange solution is produced and the solution turns red on exposure to air (distinction from 1 : 2-dihydroxyanthranol).

Melting range : Between 176° and 181°, Appendix 5.11.

Light absorption : *Extinction* of a 1-cm layer of a 0.001 per cent w/v solution in *chloroform* at 354 nm, about 0.44, Appendix 5.15 A.

Dihydroxyanthracene : Dissolve 0.1 g in 5 ml of hot *benzene*; a clear yellow or orange solution is produced.

Dihydroxyanthraquinone : Dissolve 1 mg in a few drops of *sulphuric acid*; a clear orange solution with no trace of violet colour is produced.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

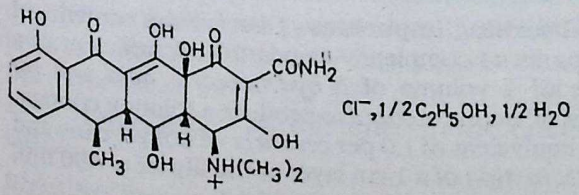
Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 20 mg, dissolve in warm *glacial acetic acid*, cool, add sufficient *glacial acetic acid* to produce 100.0 ml. Dilute 10.0 ml to 50.0 ml with *glacial acetic acid*. To 5.0 ml add 1 ml of a freshly prepared 5 per cent w/v solution of *sodium nitrite*, heat in a water-bath for two minutes, cool rapidly and add sufficient *glacial acetic acid* to produce 25.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 450 nm, within ten minutes of adding the sodium nitrite solution, Appendix 5.15 A. Calculate the content of $C_{14}H_{10}O_3$, taking 550 as the value of E(1 per cent, 1-cm) at the maximum at about 450 nm.

Storage : Store in well-closed, light-resistant containers.

Doxycycline Hydrochloride

Doxycycline Hyclate



$C_{22}H_{24}N_2O_8$, HCl, $\frac{1}{2}C_2H_5OH$, $\frac{1}{2}H_2O$ Mol. Wt. 512.95

Category : Antibacterial.

Dose : Initial, the equivalent of 0.2 g of doxycycline; subsequent doses, the equivalent of 0.1 g of doxycycline daily.

Description : Yellow, crystalline powder; odour, slightly ethanoiic; taste, bitter.

Solubility : Freely soluble in *water* and in *methyl alcohol*; practically insoluble in *chloroform* and in *solvent ether*.

Standards : Doxycycline Hydrochloride is the hemihydrate, hemiethanolate of (4*S*, 4a*R*, 5*S*, 5a*R*, 6*R*, 12a*S*)-*N*-(2-carbamoyl-1, 4, 4a, 5, 5a, 6, 11, 12a-octahydro-3, 5, 10, 12, 12a-pentahydroxy-6-methyl-1, 11-dioxonaphthacen-4-yl)-*N*, *N*-dimethyl ammonium chloride, an antimicrobial substance obtained from oxytetracycline or methacycline. It contains the equivalent of not less than 800 µg and not more than 920 µg of doxycycline, $C_{22}H_{24}N_2O_8$ per mg.

Identification : (A) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using a coating substance prepared as follows: Boil 50 g of *kieselguhr G* with a mixture of 250 ml of *hydrochloric acid* and 250 ml of *water* for ten minutes, filter, and wash the filter with *water* until the washings are alkaline to *congo red solution*; dry the residue at 105°, and slurry 25 g with a mixture of 2.5 ml of a 20 per cent v/v solution of *polyethylene glycol 400* in *glycerol* and 47.5 ml of *0.1M disodium ethylenediaminetetraacetate* previously adjusted to pH 7 with *dilute ammonia solution*. After spreading the plate, allow to dry at room temperature until the surface acquires a uniform matt appearance (usually after about one to two hours), and place in a tank whose atmosphere has been allowed to equilibrate with a saturated solution of *ammonium chloride* for at least twenty-four hours before hand. Allow the plate to remain in the tank for twenty-four hours and use immediately after removal.

Use as the mobile phase *ethyl acetate* saturated with *0.1M disodium ethylenediaminetetraacetate* previously adjusted to pH 7 with *dilute ammonia solution*. Apply separately to the plate 1 µl of each of two freshly prepared solutions in *methyl alcohol* containing (1) 0.05 per cent w/v of the substance being examined and (2) 0.05 per cent w/v of *doxycycline hydrochloride R.S.* After removal of the plate, allow it to dry in air, expose to the vapour of *strong ammonia solution*, and examine under an ultra-violet lamp having a maximum output at about 366 nm. The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

(B) To 0.5 mg add 2 ml of *sulphuric acid*; a yellow colour is produced.

(C) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Light absorption : *Extinction* of a 1-cm layer of a 0.001 per cent w/v solution in a mixture of 1 volume of *N hydrochloric acid* and 99 volumes of *methyl alcohol* at 349 nm, between 0.28 and 0.31, Appendix 5.15 A.

pH : Between 2.0 and 3.0, determined in a 1.0 per cent w/v solution, Appendix 5.10.

Light absorbing impurities : *Extinction* of a 1-cm layer of a 1.0 per cent w/v solution in a mixture of 1 volume of *N hydrochloric acid* and 99 volumes of *methyl alcohol* at 490 nm, not greater than 0.12, Appendix 5.15 A.

Ethyl alcohol : Between 4.3 per cent and 6.0 per cent w/w of C_2H_6O, determined by the following method : Carry out the method for *gas-liquid chromatography*, Appendix 5.4.1, using solutions in *water* containing (1) 0.05 per cent v/v of *ethyl alcohol* and 0.05 per cent v/v of *n-propyl alcohol* (internal standard), (2) 1.0 per cent w/v of the substance being examined, and (3) 1.0 per cent w/v of the substance being examined and 0.05 per cent v/v of the internal standard. The chromatographic procedure may be carried out using (a) a column 1.5 m long and 5 nm in internal diameter packed with porous polymer beads (80 to 100 mesh) maintained at 135°, (b) nitrogen as the carrier gas, and (c) a flame ionisation detector. Calculate the percentage w/w of C_2H_6O, assuming the weight per ml at 20° to be 0.79 g.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using the coating and method of equilibrating the plate described in **Identification** test (A). Use as the mobile phase *ethyl acetate* saturated with *0.1M disodium ethylenediaminetetraacetate* previously adjusted to pH 7 with *dilute ammonia solution*. Apply separately to the plate 1 µl of each of four freshly prepared solutions in *methyl alcohol* containing (1) 1.0 per cent w/v of the substance being examined, (2) 0.01 per cent w/v of *oxytetracycline hydrochloride R.S.*, (3) 0.02 per cent w/v of *6-epidoxycycline hydrochloride R.S.*, and (4) 0.02 per cent w/v of *methacycline hydrochloride R.S.* After removal of the plate allow it to dry in air, expose to the vapour of *strong ammonia solution*, and examine under an ultraviolet lamp having a maximum output at about 366 nm. Any spots in the chromatogram obtained with solution (1), other than the principal spot, are not more intense than the corresponding spots in the chromatogram obtained with solutions (2), (3) and (4).

Fluorine : Burn 0.30 g in three equal portions, by the *oxygen-flask method*, Appendix 3.3.6, using a 1-litre flask and a fresh 20-ml portion of *water* for each combustion, shaking the flask vigorously for about fifteen minutes, and transferring to a 100-ml *Nessler cylinder* between successive combustions. Add 5 ml of *acid zirconyl alizarin solution*, adjust the volume to 100 ml with *water*, and allow to stand for one hour. The colour of the solution so obtained is greater than that obtained by repeating the operation with no substance enclosed in the successive portions of filter paper burnt in the *oxygen-flask method*, but adding 1 ml of a 0.0066 per cent w/v solution of *sodium fluoride* to the combined absorption liquid before adding the *acid zirconyl alizarin solution*.

Undue toxicity : Complies with the test described under Bacitracin, using 0.5 ml of a solution containing 5 mg per ml in *saline solution*.

Sulphated ash : Not more than 0.4 per cent, Appendix 3.2.7.

Water : Between 1.4 per cent and 2.8 per cent w/w, Appendix 3.3.25.

Assay : Carry out the *microbiological assay of antibiotics, Method B*, Appendix 4.1, and express the results in µg of doxycycline per mg.

Storage : Store in tightly-closed, light-resistant containers.

Labelling : The label on the container states (1) the date after which the contents are not intended to be used; (2) the storage conditions.

Doxycycline Capsules

Category : Antibacterial.

Dose : Initial dose, the equivalent of 0.2 g of doxycycline; subsequent doses, the equivalent of 0.1 g of doxycycline daily.

Usual strengths : 50 mg; 100 mg; 200 mg.

Standards : Doxycycline Capsules contain a quantity of Doxycycline Hydrochloride equivalent to not less than 90.0 per cent and not more than 120.0 per cent of the stated amount of doxycycline, $C_{22}H_{24}N_2O_8$.

Identification : (A) The contents of the capsules comply with **Identification** test (A) described under Doxycycline Hydrochloride solution (1) being freshly prepared by extracting a quantity equivalent to 10 mg of doxycycline with 20 ml of *methyl alcohol*, centrifuging and using the supernatant liquid.

(B) The contents of the capsules comply with **Identification** tests (B) and (C) described under Doxycycline Hydrochloride.

Light absorbing impurities : Dissolve the contents of five capsules as completely as possible in sufficient of a mixture of 1 volume of *N hydrochloric acid* and 99 volumes of *methyl alcohol* to produce a solution containing the equivalent of 1.0 per cent w/v of doxycycline and filter. *Extinction* of a 1-cm layer of the filtrate at 490 nm, not greater than 0.2, Appendix 5.15 A.

Loss on drying : Not more than 8.5 per cent, determined

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

on 0.5 g of the contents of the capsules by drying in an oven at 105° for two hours, Appendix 5.8.

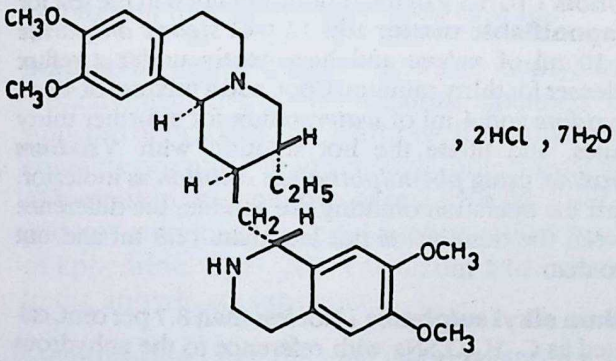
Other requirements : Comply with the requirements stated under Capsules.

Assay : Weigh accurately a quantity of the contents equivalent to 0.2 g of doxycycline, add 200 ml of *0.1N hydrochloric acid*, shake and filter. On the filtrate carry out the *microbiological assay of antibiotics, Method A*, Appendix 4.1.

Storage : Store in tightly-closed, light-resistant containers.

Labelling : The label on the container states (1) the strength in terms of the equivalent amount of doxycycline; (2) the date after which the capsules are not intended to be used; (3) the storage conditions.

Emetine Hydrochloride



$C_{29}H_{40}N_2O_4$, 2HCl, $7H_2O$ Mol. Wt. 679.57

Category : Anti-amoebic.

Dose : By subcutaneous or intramuscular injection, 30 to 60 mg daily.

Description : White or very slightly yellowish crystalline powder; odourless; taste, bitter. Develops a faint-yellow tint on exposure to light.

Solubility : Freely soluble in *water* and in *alcohol*.

Standards : Emetine Hydrochloride is the heptahydrate of the dihydrochloride of 6′, 7′, 10, 11-tetramethoxyemetan (emetine) obtained from Ipecacuanha cephaëline or prepared synthetically. It contains not less than 98.0 per cent and not more than the equivalent of 101.5 per cent of $C_{29}H_{40}N_2O_4$, 2HCl, calculated with reference to the dried substance.

Identification : (A) Add 2 mg to 1 ml of *sulphuric acid* containing about 5 mg of *molybdic acid*, a bright green colour develops.

(B) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

Acidity : Dissolve 0.1 g in 10 ml of *water*, and 1 drop of *methyl red solution* and titrate with *0.02N sodium hydroxide*; not more than 0.5 ml is required.

Specific optical rotation : Between +17.0° and +18.3°, calculated with reference to the dried substance and determined in a 6 per cent w/v solution, Appendix 5.12.

Other alkaloids : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 100 volumes of *chloroform*, 5 volumes of *methyl alcohol*, 20 volumes of *2-methoxyethanol*, 2 volumes of *water* and 0.5 volume of *diethylamine*, as the mobile phase. Apply separately to the plate, ensuring that the diameters of the spots do not exceed 6 mm, 5 µl of each of four freshly prepared solutions in a 1 per cent v/v solution of *dilute ammonia solution* in *methyl alcohol* containing: (1) 0.05 per cent w/v of the substance being examined; (2) 0.001 per cent w/v of *isoemetine hydrochloride R.S.*; (3) 0.00025 per cent w/v of *O-methylpsychotrine R.S.*; and (4) 0.001 per cent w/v of *cephaeline hydrochloride R.S.* After removal of the plate, allow it to dry in air until the odour of the solvent is no longer detectable, spray with a 0.5 per cent w/v solution of *iodine* in *chloroform*, heat at 60° for fifteen minutes, and examine under an ultra-violet lamp having a maximum output at about 366 nm. The chromatogram obtained with solution (1) may show subsidiary spots corresponding to either O-methylpsychotrine and isoemetine hydrochloride, or to O-methylpsychotrine and cephaeline hydrochloride. The intensity of the subsidiary spots is not greater than that of the corresponding spots in the appropriate chromatograms.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Between 15.0 per cent and 19.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.2 g and dissolve in 20 ml of *water*, add 10 ml of *sodium hydroxide solution*, shake with successive quantities, each of 50 ml, of *solvent ether* until complete extraction of the alkaloid is effected, collect the ether solutions and wash with successive quantities, each of 10 ml, of *water* until the washings, after extraction with a further 50 ml of *solvent ether*, are neutral to *litmus paper*. Mix the ethereal solutions, add 20 ml of *water* and 10.0 ml of *0.1N sulphuric acid*, shake, allow to separate and collect the aqueous layer. Shake the ethereal solution with two further quantities, each of 20 ml, of *water*, mix the aqueous solutions and titrate with *0.1N sodium hydroxide* using *methyl red solution* as indicator. Each ml of *0.1N sulphuric acid* is equivalent to 0.02768 g of $C_{29}H_{40}O_4N_2$, 2HCl.

Storage : Store in well-closed, light-resistant containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Emetine Injection

Emetine Hydrochloride Injection

Category : Anti-amoebic.

Dose : Emetine Hydrochloride, by intramuscular or subcutaneous injection, 30 to 60 mg daily.

Usual strength : 60 mg in 1 ml.

Standards : Emetine Injection is a sterile solution of Emetine Hydrochloride in Water for Injection. It contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Emetine Hydrochloride, $C_{29}H_{40}N_2O_4$, 2HCl, $7H_2O$.

Identification : (A) Evaporate 1 ml on a water-bath to dryness; the residue complies with **Identification** test (A) described under Emetine Hydrochloride.

(B) It gives the reactions of *chlorides*, Appendix 3.1.

pH : Between 2.7 and 4.0, Appendix 5.10.

Other requirements : Complies with the requirements stated under Injections.

Assay : Measure accurately a volume equivalent to about 0.2 g of Emetine Hydrochloride, and dilute with *water* to 20 ml and complete the **Assay** described under Emetine Hydrochloride, beginning at the words "add 10 ml of *sodium hydroxide solution*". Each ml of *0.1N sulphuric acid* is equivalent to 0.03398 g of $C_{29}H_{40}N_2O_4$, 2HCl, $7H_2O$.

Storage : Store in single-dose or multiple-dose, light-resistant containers.

Emulsifying Wax

Anionic Emulsifying Wax

Category : Pharmaceutical aid (emulsifying agent).

Description : Almost white, or pale yellow, waxy solid or flakes. It becomes plastic when warm; odour, faint, and characteristic.

Solubility : Practically insoluble in *water*, forming an emulsion; slightly soluble in *alcohol*.

Standards : Emulsifying Wax is a waxy solid prepared from 90 parts of Cetostearyl Alcohol, 10 parts of Sodium Lauryl Sulphate or similar sodium salts of sulphated higher primary aliphatic alcohols, and 4 parts of Purified Water.

Identification : The residue obtained in the test for **Unsaponifiable matter** melts at about 52°, Appendix 5.11.

Acidity : Weigh accurately about 20 g, add 250 ml of *alcohol*, previously neutralised to *phenolphthalein solution*. Warm gently on a water-bath until solution is effected. Titrate with *0.02N sodium hydroxide*, shaking vigorously and keeping the solution warm, until a pink colour which persists for at least fifteen seconds is obtained; not more than 0.25 ml of *0.02N sodium hydroxide* is required for each g of the substance taken.

Alkalinity : Disperse 5 g in 25 ml of warm *alcohol*, previously neutralised to *phenolphthalein solution*, and cool. Add a further 0.5 ml of *phenolphthalein solution*; the solution remains colourless.

Iodine value : Not more than 3.0, Appendix 3.3.18.

Saponification value : Not more than 2.0, Appendix 3.3.20.

Unsaponifiable matter : Between 88.0 and 92.0 per cent, Appendix 3.3.21, using about 5 g of the substance, accurately weighed, and omitting the titration of the residue.

Alcohols : To 3.5 g of the residue obtained in the test for **Unsaponifiable matter** add 12 g of *stearic anhydride* and 10 ml of *xylene* and heat gently under a reflux condenser for thirty minutes. Cool, add a mixture of 40 ml of *pyridine* and 4 ml of *water*, reflux for a further thirty minutes, and titrate the hot solution with *N sodium hydroxide*, using *phenolphthalein solution* as indicator. Repeat the operation omitting the residue; the difference between the titrations is not less than 12.8 ml and not more than 14.2 ml.

Sodium alkyl sulphates : Not less than 8.7 per cent, calculated as $C_{12}H_{25}O_4SNa$ with reference to the anhydrous substance, and determined by the following method: Weigh accurately about 0.25 g and dissolve as completely as possible in 15 ml of *chloroform*, add 30 ml of *water*, 10 ml of *dilute sulphuric acid* and 1 ml of *dimethyl yellow-oracet blue B solution* and titrate with *0.004M benzethonium chloride*, shaking vigorously and allowing the layers to separate after each addition, until the chloroform layer acquires a permanent clear green colour. Each ml of *0.004M benzethonium chloride* is equivalent to 0.001154 g of sodium alkyl sulphates, calculated as $C_{12}H_{25}O_4SNa$.

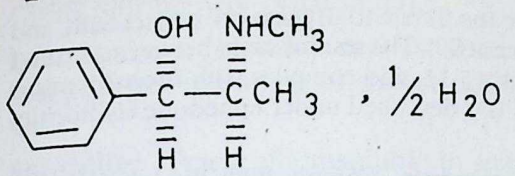
Water : Not more than 4.0 per cent w/w, Appendix 3.3.25.

Storage : Store in well-closed containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Ephedrine



$C_{10}H_{15}NO,\frac{1}{2}H_2O$ Mol. Wt. 174.24 (hemihydrate)
$C_{10}H_{15}NO$ 165.23 (anhydrous)

Category : Adrenergic (bronchodilator).

Dose : 15 to 60 mg.

Description : Almost colourless, hexagonal, prismatic crystals or white crystalline powder; odourless or has a slight, unpleasant smell; taste, bitter. It gradually decomposes on exposure to light.

Solubility : Soluble in *water*, in *alcohol*, in *solvent ether* and in *chloroform*; dissolves slowly in *liquid paraffin*. With the hemihydrate, solutions in *chloroform* may show separation of water.

Standards : Ephedrine is (1*R*, 2*S*)-2-methylamino-1-phenylpropan-1-ol, an alkaloid obtained from *Ephedra* or prepared by synthesis. It is anhydrous or contains not more than one-half molecule of water of hydration. It contains not less than 98.5 per cent and not more than the equivalent of 100.5 per cent of Ephedrine, $C_{10}H_{15}NO$, calculated with reference to the anhydrous substance.

Identification : (A) The light absorption, in the range 220 to 350 nm, of a 1-cm layer of a 0.05 per cent w/v solution in *0.1N hydrochloric acid* exhibits maxima at about 251 nm, 259 nm, and 265 nm; *extinction* at 251 nm, about 0.4; at 259 nm, about 0.47; and at 265 nm, about 0.35, Appendix 5.15 A.

(B) Dissolve 10 mg in 1 ml of *water*, add 0.2 ml of *dilute hydrochloric acid* and add 0.1 ml of *copper sulphate solution* followed by 1 ml of *sodium hydroxide solution*; the liquid becomes violet. Add 1 ml of *solvent ether* and shake; the ethereal layer is purple and the aqueous layer is blue.

Melting range : Between 40° and 43° (hydrated material) determined on the undried substance, Appendix 5.11. The anhydrous material melts at about 38°.

Clarity and colour of solution : A 2.5 per cent w/v solution is clear and colourless.

Specific optical rotation : Between −41° and −43°, determined at 20° in a solution prepared by dissolving 2.25 g in 15 ml of *dilute hydrochloric acid* and diluting to 50.0 ml with *water*, Appendix 5.12.

Chloride : Dissolve 0.1 g in 1 ml of *water* and 1 ml of *dilute nitric acid* and add 0.1 ml of *silver nitrate solution*; no turbidity is produced.

Sulphate : Dissolve 0.1 g in 1 ml of *water* and 1 ml of *dilute hydrochloric acid* and add 0.5 ml of *barium chloride solution*; no turbidity is produced within ten minutes.

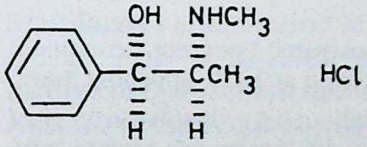
Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Water : Between 4.5 per cent and 5.5 per cent w/w (for hemihydrate) and not more than 1.0 per cent w/w (for anhydrous), Appendix 3.3.25.

Assay : Weigh accurately about 0.5 g, dissolve in 5 ml of *alcohol*. Add 50.0 ml of *0.1N hydrochloric acid* and titrate with *0.1N sodium hydroxide*, using *methyl red solution* as indicator. Each ml of *0.1N hydrochloric acid* is equivalent to 0.01652 g of $C_{10}H_{15}NO$.

Storage : Store in well-closed, light-resistant containers.

Ephedrine Hydrochloride



$C_{10}H_{15}NO,HCl$ Mol. Wt. 201.70

Category : Adrenergic (bronchodilator).

Dose : 15 mg to 60 mg.

Description : Colourless crystals or powder; odourless; taste, bitter. It is affected by light.

Solubility : Freely soluble in *water*; soluble in *alcohol*; practically insoluble in *solvent ether*.

Standards : Ephedrine Hydrochloride is hydrochloride of (1*R*, 2*S*)-2-methylamino-1-phenyl-1-propanol. It contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of $C_{10}H_{15}NO,HCl$, calculated with reference to the dried substance.

Identification : (A) The light absorption, in the range 220 to 350 nm, of a 1-cm layer of a 0.05 per cent w/v solution exhibits maxima at about 252 nm, 259 nm and 265 nm; *extinction* of 252 nm, about 0.4; at 259 nm, about 0.47; at 265 nm, about 0.35, Appendix 5.15 A.

(B) Dissolve 10 mg in 1 ml of *water*, and add 0.1 ml of *copper sulphate solution* and 1 ml of *sodium hydroxide solution*; the liquid becomes violet in colour; add 1 ml of *solvent ether* and shake; the ethereal layer is purple and the aqueous layer is blue.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

(C) Dissolve about 50 mg in 1 ml of *water*, add 4 ml of *0.1N sodium hydroxide* and 3 ml of *carbon tetrachloride*, shake for a few seconds and allow to stand for two minutes. Separate the organic phase, add a few *copper turnings* and shake. A turbidity appears rapidly and after few minutes a copious precipitate is obtained.

(D) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

Melting range : Between 217° and 220°, Appendix 5.11.

Clarity and colour of solution : A 10.0 per cent w/v solution is clear or not more than very slightly opalescent and colourless.

Specific optical rotation : Between –33.5° and –35.5° determined in a 5 per cent w/v solution, Appendix 5.12.

Acidity or Alkalinity : Dissolve 0.2 g in 10 ml of freshly boiled and cooled *water* and titrate with *0.02N sodium hydroxide* or *0.02N hydrochloric acid*, using *methyl red solution* as indicator; not more than 0.1 ml of *0.02N sodium hydroxide* or *0.02N hydrochloric acid* is required.

Sulphates : 15 ml of a 10 per cent w/v solution complies with the *limit test for sulphates*, Appendix 3.2.8.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.5 g, dissolve in 25 ml of *glacial acetic acid*, add 10 ml of *mercuric acetate solution* and titrate with *0.1N perchloric acid*, using *crystal-violet solution* as indicator, until the colour changes from blue to green-blue. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02017 g of $C_{10}H_{15}NO$, HCl.

Storage : Store in well-closed, light-resistant containers.

Ephedrine Tablets

Ephedrine Hydrochloride Tablets

Category : Adrenergic (bronchodilator).

Dose : 15 to 60 mg.

Usual strengths : 15 mg; 30 mg; 60 mg.

Standards : Ephedrine Hydrochloride Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Ephedrine Hydrochloride, $C_{10}H_{15}NO$, HCl.

Identification : (A) Triturate a quantity of the powdered tablets, equivalent to about 0.4 g of Ephedrine Hydrochloride, with 20 ml of warm *alcohol* for twenty minutes, filter, evaporate the filtrate to dryness on a water-bath, and dry the residue at 80°. The residue melts between 217° and 220°, Appendix 5.11, and complies with **Identification** tests (B) and (D) described under Ephedrine Hydrochloride.

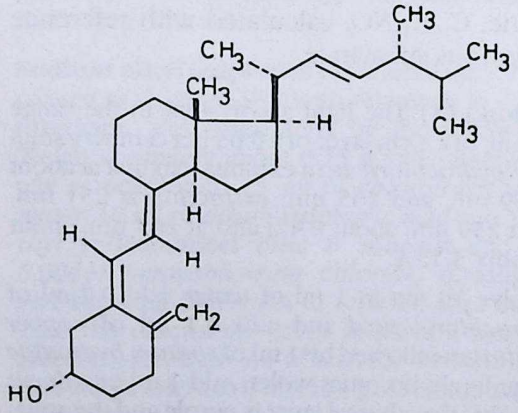
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh 20 tablets and reduce to a *fine powder*. Weigh accurately a quantity of the powder equivalent to about 0.15 g of Ephedrine Hydrochloride and add 30 ml of *glacial acetic acid*, 10 ml of *mercuric acetate solution* and 0.1 ml of *crystal-violet solution*. Warm gently to effect solution, cool, and titrate with *0.1N perchloric acid* until the violet colour changes to green-blue. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent 0.02017 g of $C_{10}H_{15}NO$,HCl.

Storage : Store in well-closed, light-resistant containers.

Ergocalciferol

Calciferol; Vitamin D_2



$C_{28}H_{44}O$ Mol. Wt. 396.65

Category : Vitamin D (antirachitic).

Dose : In the prevention of rickets, not more than 20 μg (800 Units) daily, allowance being made for Vitamin D obtained from other sources.

In the treatment of rickets and osteomalacia, 0.125 to 1.25 mg (5000 to 50,000 Units) daily.

In the treatment of hypoparathyroidism, 1.25 to 5 mg (50,000 to 200,000 Units) daily.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Calciferol contains in 1 mg, 40,000 Units of antirachitic activity (Vitamin D).

Description : Colourless crystals or white, crystalline powder; odourless or almost odourless; tasteless.

Solubility : Practically insoluble in *water*; soluble in *alcohol*, in *chloroform*, in *solvent ether*, and slightly soluble in fixed oils.

Standards : Ergocalciferol is (5*Z*, 7*E*)-(3*S*)-9,10-secoergosta-5, 7, 10(19), 22-tetraen-3-ol.

Identification : (A) The light absorption, in the range 230 to 350 nm, of the solution prepared in the test for Light absorption, exhibits a maximum only at 265 nm, Appendix 5.15 A.

(B) Dissolve 0.5 g in 1 ml of dry *pyridine*; dissolve 0.5 g of *dinitrobenzoyl chloride* in 2 ml of dry *pyridine* by warming on a water-bath; mix the solutions and warm on a water-bath for ten minutes. Add 5 ml of *water* to the hot solution, filter and wash the precipitate with *water*. Dissolve in 10 ml of hot *acetone*, cool, and allow to stand for a short time, filter, wash the residue with a little cold *acetone*, and dry in a vacuum desiccator; the residue melts at about 148°, Appendix 5.11; *specific optical rotation*, in solution in *benzene*, about +58°, Appendix 5.12.

Melting range : Between 115° and 118°, Appendix 5.11.

Specific optical rotation : Between +103° and +106°, determined in a 1.5 per cent w/v solution in *ethyl alcohol*, Appendix 5.12. The solution should be prepared without delay from a container opened no longer than thirty minutes and the rotation should be determined within thirty minutes of preparing the solution.

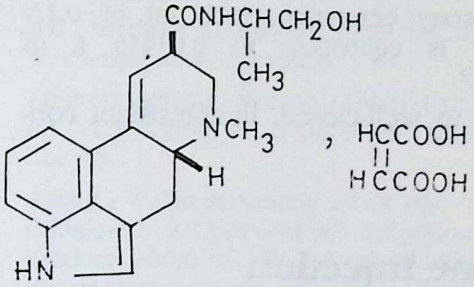
Light absorption : *Extinction* of a 1-cm layer of a 0.001 per cent w/v solution in *cyclohexane* at the maximum at about 265 nm, not less than 0.460, Appendix 5.15 A.

Reducing substances : To 10 ml of a 1.0 per cent w/v solution in *ethyl alcohol*, add 0.5 ml of a 0.5 per cent w/v solution of *blue tetrazolium* in *ethyl alcohol*. Add 0.5 ml of a solution prepared by diluting 1 volume of *tetramethylammonium hydroxide solution (10 per cent)* with *ethyl alcohol* to make 10 volumes. Allow to stand for five minutes, accurately timed, and then add 1 ml of *glacial acetic acid*. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 525 nm, using *ethyl alcohol* as the blank, Appendix 5.15A. The *extinction* is not greater than the *extinction* obtained by carrying out the test simultaneously on a solution containing 0.2 µg per ml of *hydroquinone* in *ethyl alcohol*.

Storage : Store in hermetically sealed light-resistant containers under nitrogen, at a temperature not exceeding 15°

Ergometrine Maleate

Ergonovine Maleate



$C_{19}H_{23}N_3O_2, C_4H_4O_4$ Mol. Wt. 441.48

Category : Oxytocic.

Dose : By intramuscular injection, 0.2 to 1 mg; by intravenous injection, 0.1 to 0.5 mg.

Description : White or faintly yellow, crystalline powder; odourless. It is affected by light.

Solubility : Sparingly soluble in *water* and in *alcohol*; practically insoluble in *chloroform* and in *solvent ether*.

Standards : Ergometrine Maleate is the hydrogen maleate of 9, 10-didehydro-*N*-[(*S*)-2-hydroxy-1-methylethyl]-6-methylergoline-8β-carboxamide, an alkaloid obtained from ergot. It contains not less than 97.0 per cent and not more than the equivalent of 103.0 per cent of $C_{19}H_{23}N_3O_2, C_4H_4O_4$, calculated with reference to the dried substance.

Identification : (A) To 0.1 g add 4 ml of freshly boiled *water* and make upto 10 ml with *water*. The solution has a blue fluorescence.

(B) To 2 drops of solution obtained in **Identification** test A add 1 ml of *glacial acetic acid*, 1 drop of *ferric chloride solution* and 1 ml of *phosphoric acid*. After a few minutes the mixture becomes blue or violet.

(C) Dissolve about 2 mg in 20 ml of *water*; to 1 ml of this solution add 2 ml of *dimethylaminobenzaldehyde solution*; after about ten minutes the mixture exhibits a deep blue colour.

Melting range : Between 195° and 197°, with decomposition, Appendix 5.11.

Specific optical rotation : Between +50° and +56°, determined in a 1.0 per cent w/v solution, Appendix 5.12.

pH : Between 3.0 and 5.0, determined in a 1.0 per cent w/v solution, Appendix 5.10.

Related substances : Complies with the test described under Methylergometrine Maleate, using *ergometrine maleate R.S.*, instead of *methylergometrine maleate R.S.*

Loss on drying : Not more than 2.0 per cent, determined on 1.0 g by drying "in vacuo at 80°", Appendix 5.8.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Assay : Weigh accurately about 0.1 g and dissolve in 10 ml of *glacial acetic acid* and 10 ml of *acetic anhydride* and titrate with *0.1N perchloric acid*, using *crystal-violet solution* as indicator. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.04415 g of $C_{19}H_{23}N_3O_2,C_4H_4O_4$.

Storage : Store in well-closed, light-resistant containers.

Ergometrine Injection

Ergometrine Maleate Injection

Ergonovine Maleate Injection

Category : Oxytocic.

Dose : Ergometrine Maleate, by intramuscular injection, 0.2 to 1 mg, by intravenous injection, 0.1 to 0.5 mg.

Usual strength : 0.5 mg in 1 ml.

Description : Colourless or faintly yellow, clear solution.

Standards : Ergometrine Injection is a sterile solution of Ergometrine Maleate in Water for Injection containing suitable stabilisers. It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of $C_{19}H_{23}N_3O_2,C_4H_4O_4$.

Identification : (A) The solution exhibits a blue fluorescence.

(B) To volume equivalent to 0.1 mg of Ergometrine Maleate, add 0.5 ml of *water* and 2 ml of *dimethylaminobenzaldehyde solution*; after about ten minutes the mixture exhibits a blue colour.

pH : Between 2.7 and 3.5, Appendix 5.10.

Related substances : Complies with the test described under Methylergometrine Injection, using *ergometrine maleate R.S.* instead of *methylergometrine maleate R.S.* and preparing solution (1) using a volume of the injection equivalent to 1 mg of Ergometrine Maleate.

Other requirements : Complies with the requirements stated under Injections.

Assay : Protect the solutions from light throughout the assay . To an accurately measured volume add sufficient *water* to produce a solution containing 0.04 mg of Ergometrine Maleate per ml. To 3.0 ml add 6.0 ml of *dimethylaminobenzaldehyde solution*, mix, cool to room temperature and allow to stand for 30 minutes (*solution A*). At the same time prepare two solutions as follows :

Solution B—To 3.0 ml of 0.004 per cent w/v solution of *ergometrine maleate R.S.* add 6.0 ml of *dimethylaminobenzaldehyde solution*, mix, cool to room temperature and allow to stand for thirty minutes.

Solution C —Mix 6.0 ml of *dimethylaminobenzaldehyde solution*, with 3.0 ml of *water*. Measure the *extinction* of a 1-cm layer of solution B at the maximum at about 545 nm, Appendix 5.15 A, using solution C as the blank. Without delay replace solution B with solution A, using the same cell and measure the *extinction* of solution A at the same wavelength. Each mg of *ergometrine maleate R.S.* is equivalent to 1.000 mg of $C_{23}H_{27}N_3O_6$.

Storage : Store in single-dose, light-resistant containers in a cool place.

Ergometrine Tablets

Ergometrine Maleate Tablets

Ergonovine Maleate Tablets

Category : Oxytocic.

Dose : Ergometrine Maleate, 0.5 to 1 mg.

Usual strengths : 0.25 mg; 0.5 mg.

Standards : Ergometrine Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of ergometrine maleate, $C_{19}H_{23}N_3O_2$, $C_4H_4O_4$.

Identification : The powdered tablets comply with **Identification** tests (A) and (C) described under Ergometrine Maleate.

Uniformity of content : Protect the solutions from light throughout the assay. Powder one tablet and add 10 ml of 1 per cent w/v solution of *tartaric acid*, shake for thirty minutes and centrifuge. Complete the **Assay** described under Ergometrine Injection, beginning at the words "Add sufficient *water* to produce a solution containing 0.04 mg of Ergometrine Maleate....." and calculate the content of $C_{23}H_{27}N_3O_6$. Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 85 and 115 per cent of the average except that for one tablet the content may be between 80 and 120 per cent of the average.

Other requirements : Comply with the requirements stated under Tablets.

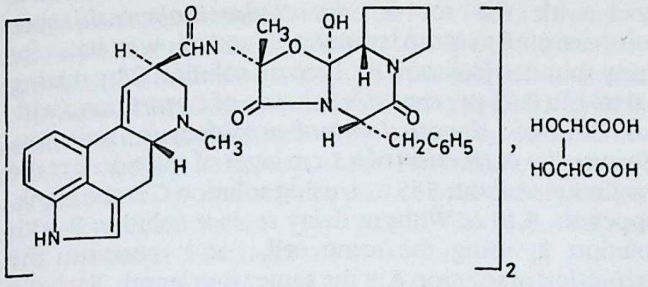
Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 2 mg of Ergometrine Maleate and dissolve in 50.0 ml of a 1 per cent w/v solution of *tartaric acid*. Complete the **Assay** described under Ergometrine Injection, beginning at the words, "To 3.0 ml add 6.0 ml of *dimethylaminobenzaldehyde solution*...."

Storage : Store in tightly-closed, light-resistant containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Ergotamine Tartrate



$(C_{33}H_{35}N_5O_5)_2, C_4H_6O_6$ Mol. Wt. 1313.43

Category : Analgesic (specific in migraine).

Dose : 1 to 2 mg.

Description : Colourless crystals, or white, or almost white crystalline powder; odourless.

Solubility : Slightly soluble in *water* and in *alcohol.*

Standards : Ergotamine Tartrate is the tartrate of (5′*R*)-12′-hydroxy-2′ methyl-3′, 6′, 18-trioxo-5- benzylergotaman, an alkaloid obtained from ergot. It contains not less than 97.0 per cent and not more than the equivalent of 103.0 per cent of $(C_{33}H_{35}N_5O_5)_2, C_4H_6O_6$ calculated with reference to the dried substance.

Identification : (A) Dissolve 1 mg in a mixture of 5 ml of *glacial acetic acid* and 5 ml of *ethyl acetate.* To 1 ml of this solution add 1 ml of *sulphuric acid,* with continuous shaking and cooling; a blue colour with a red tinge develops. Add 0.1 ml of *ferric chloride test-solution,* previously dilute with an equal volume of *water*; the red tinge becomes less apparent and the blue colour more pronounced.

(B) Dissolve 1 mg in 5 ml of a 1 per cent w/v solution of *tartaric acid.* To 1 ml of the solution add slowly 3 ml of *dimethylaminobenzaldehyde solution* and mix; a deep blue colour is produced.

(C) It softens at about 187° and decomposes at about 192° without melting, Appendix 5.11.

Specific optical rotation : Between −150° to −160°, determined by the following method: Carry out the operations in subdued light and as quickly as possible. To 0.30 g add 25ml of *water* and 0.5 g of *sodium bicarbonate.* Shake vigorously for 5 minutes with 10 ml of *alcohol-free chloroform* and filter the chloroform layer through a folded filter paper moistened with *alcohol-free chloroform.* Repeat the operation six times using 6 ml of *alcohol-free chloroform* each time and filtering the extracts through the same filter paper. Dilute the combined extracts to 50.0 ml with the same solvent and measure the *optical rotation* in a 1-dm tube at 25°, Appendix 5.12. Evaporate a known volume of the chloroform solution to dryness and dry the residue of ergotamine base to constant weight at 100°, "in vacuo", and calculate the *specific optical rotation* from the weight of the residue, Appendix 5.12.

pH : Between 4.0 and 6.0, determined in a 0.25 per cent w/v suspension, Appendix 5.10.

Loss on drying : Not more than 6.0 per cent, determined on 0.1 g drying "in vacuo at 95°" for six hours, Appendix 5.8.

Assay : Weigh accurately about 10.0 mg and dissolve in sufficient of a 1 per cent w/v solution of *tartaric acid* to produce 200.0 ml. To 3.0 ml add 6.0 ml of *dimethyl aminobenzaldehyde solution.* Allow to stand for 20 minutes in subdued light and measure the *extinction* of the resulting solution at 578 nm, Appendix 5.15 A, using a mixture of 3.0 ml of 1 per cent w/v solution of *tartaric acid* and 6.0 ml of *dimethyl aminobenzaldehyde solution* as blank. Calculate the content of $(C_{33}H_{35}N_5O_5)_2, C_4H_6O_6$ from the *extinction* obtained by repeating the operation using 6.7 mg of *ergometrine maleate R.S.* in place of the substance being examined; 6.722 mg of anhydrous ergometrine maleate, is equivalent to 10.0 mg of anhydrous ergotamine tartrate.

Storage : Store in light-resistant, sealed tube, under nitrogen and in a cool place.

Ergotamine Injection

Ergotamine Tartrate Injection

Category : Analgesic (specific in migraine).

Dose : Ergotamine Tartrate. By subcutaneous or intramuscular injection, 0.25 to 0.5 mg.

Usual strength : 0.5 mg in 1 ml.

Description : Colourless or almost colourless solution.

Standards : Ergotamine Injection is a sterile solution of Ergotamine Tartrate in Water for Injection. It may contain Alcohol, Glycerin and sufficient Tartaric Acid to adjust the pH of the solution to 3.3. It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of total alkaloids, of which not less than 50.0 per cent and not more than 70.0 per cent is present as ergotamine tartrate.

Identification : (A) To a volume equivalent to 0.2 mg of Ergotamine Tartrate, add 1 ml of *dimethylaminobenzaldehyde solution*; a deep blue colour is produced.

(B) Mix a volume equivalent to 2 mg of Ergotamine Tartrate with 2 ml of *dilute sulphuric acid,* dissolve a few

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

mg of *magnesium powder* in the solution, add 25 mg of *resorcinol*. Shake to dissolve and carefully add 2 ml of *sulphuric acid* down the inside of the tube and warm gently. A red ring forms at the interface of the two liquid layers and spreads throughout the lower layer.

pH : Between 2.8 and 3.8, Appendix 5.10.

Ergot alkaloids and related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* slurried with *0.1N sodium hydroxide* as the coating substance and a mixture of 9 volumes of *chloroform* and 1 volume of *methyl alcohol* as the mobile phase. Prepare two solutions as follows : (1) To a volume of the injection equivalent to 5 mg of Ergotamine Tartrate add sufficient of a 10 per cent w/v solution of *sodium bicarbonate* to make it distinctly alkaline to *litmus paper*. Extract with five quantities, each of 10 ml, of *chloroform*, filter the extracts through a small double filter paper, wash the filter with *chloroform*, evaporate the combined filtrates and washings to dryness at 20° "in vacuo", and dissolve the residue in 1.0 ml of a mixture of equal volumes of *methyl alcohol* and *chloroform*.

(2) Dissolve 5 mg of *ergotamine tartrate R.S.* in 10 ml of a 1 per cent w/v solution of *tartaric acid* and complete the preparation described for solution (1) beginning at the words "Extract with five quantities .....". Without delay, apply separately to the plate 20 µl and 2 µl of solution (1) and 14 µl, 10 µl, 7 µl and 2 µl of solution (2).

After removal of the plate, allow it to dry in air and examine under an ultra-violet lamp having a maximum output at about 366 nm. The chromatogram obtained with 20 µl of solution (1) shows two principal spots, corresponding to ergotamine and, above it, ergotaminine; a spot between the two principal spots and a number of spots below them may also be seen.

Compare the chromatogram obtained from 20 µl of solution (1) with the chromatograms obtained from solution (2). The spot corresponding to ergotaminine is not larger or more intense than the spot corresponding to ergotamine obtained from 7 µl of solution (2); the spot corresponding to ergotamine is not smaller or less intense than the spot corresponding to ergotamine obtained from 10 µl of solution (2) and is not larger or more intense than the spot corresponding to ergotamine obtained from 14 µl of solution (2), corresponding to not less than 50 per cent and not more than 70 per cent of ergotamine tartrate. Any other spots are not larger or more intense than the spot corresponding to ergotamine obtained from 2 µl of solution (2).

Other requirements : Complies with the requirements stated under Injections.

Assay : To an accurately measured volume add sufficient of 0.25 per cent w/v solution of *tartaric acid* to produce a solution containing 0.05 mg of Ergotamine Tartrate per ml, mix 3.0 ml with 6.0 ml of *dimethylaminobenzaldehyde solution*, cool to room temperature, and allow to stand for thirty minutes (solution A). At the same time mix 3.0 ml of a 0.003 per cent w/v solution of *ergometrine maleate R.S.* in a 0.25 per cent w/v solution of *tartaric acid* with 6.0 ml of *dimethylaminobenzaldehyde solution*, cool to room temperature and allow to stand for thirty minutes (solution B). Prepare solution C by mixing 3.0 ml of a 0.25 per cent w/v solution of *tartaric acid* with 6.0 ml of *dimethylaminobenzaldehyde solution*. Measure the *extinction* of a 1-cm layer of solution B at the maximum at about 545 nm, using solution C as the blank, Appendix 5.15 A. Without delay replace solution B with solution A, using the same cell, and measure the *extinction* of solution A at the same wavelength. Each mg of *ergometrine maleate R.S.* is equivalent to 1.488 mg of $(C_{33}H_{35}N_5O_5)_2, C_4H_6O_6$.

Storage : Store in single-dose, light-resistant containers.

Ergotamine Tablets

Ergotamine Tartrate Tablets

Category : Analgesic (specific in migraine).

Dose : Ergotamine Tartrate 1 to 2 mg as a single dose.

Usual strength : 1 mg.

Standards : Ergotamine Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Ergotamine Tartrate $(C_{33}H_{35}N_5O_5)_2, C_4H_6O_6$. The tablets may be coated.

Identification : Triturate a quantity of the powdered tablets equivalent to about 5 ml of Ergotamine Tartrate with 10 ml of *light petroleum (boiling range, 40° to 60°)* for a few minutes, allow to settle and discard the petroleum extract. Add to the residue 10 ml of *chloroform* saturated with *strong ammonia solution*. Triturate for a few minutes, filter and evaporate the filtrate to dryness on a water-bath; the residue so obtained complies with **Identification** tests (A) and (B) described under Ergotamine Tartrate.

Uniformity of content : To one tablet add 20.0 ml of a .1 per cent w/v solution of *tartaric acid*. Shake for thirty minutes and centrifuge. Complete the **Assay** described under Ergotamine Injection, beginning at the words "Mix 3.0 ml with 6.0 ml of *dimethylaminobenzaldehyde solution*....." and calculate the content of $(C_{33}H_{35}N_5O_5)_2, C_2H_6O_6$.

Repeat the operation using a further nine tablets and calculate the average content of the tablets. The content of each tablet is between 85 and 115 per cent of the average except that for one tablet the content may be between 80 and 120 per cent of the average.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

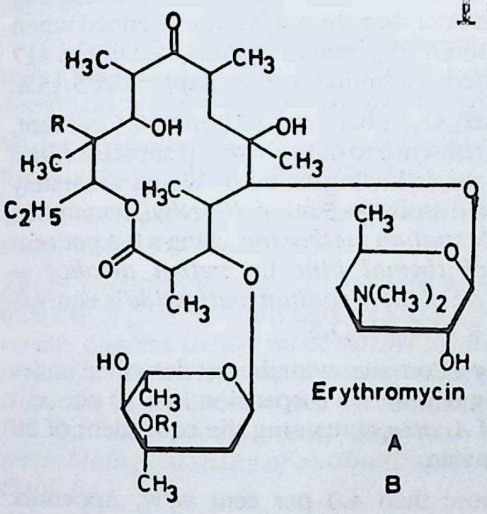
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 5 mg of Ergotamine Tartrate and dissolve in 50 ml of a 1 per cent w/v solution of *tartaric acid*, allow to stand for thirty minutes, with frequent shaking, and dilute to 100.0 ml with *water*. Complete the **Assay** described under Ergotamine Injection, using 3.0 ml of the clear supernatant liquid and beginning at the words "mix 3.0 ml with 6.0 ml of *dimethylaminobenzaldehyde solution*.....".

Storage : Store in well-closed containers.

Erythromycin

168834



Erythromycin	R	R_1
A	OH	CH_3
B	H	CH_3
C	OH	H

$C_{37}H_{67}NO_{13}$ Mol. Wt. 733.94

Category : Antibacterial.

Dose : 1 to 2 g daily, in divided doses.

Description : White or slightly yellow crystals or powder; odourless; taste, bitter. Slightly hygroscopic.

Solubility : Slightly soluble in *water*; soluble in *alcohol*, in *chloroform* and in *solvent ether*.

Standards : Erythromycin is an antimicrobial substance produced by the growth of certain strains of *Streptomyces erythreus*. It contains not less than 900 µg per mg of $C_{37}H_{67}NO_{13}$, calculated with reference to the anhydrous substances.

Identification : (A) To 5 mg add 2 ml of *sulphuric acid*, and shake gently; a reddish-brown colour is produced.

(B) Dissolve 3 mg in 2 ml of *acetone* and add 2 ml of *hydrochloric acid*; an orange colour is produced which changes to red and then to purplish-red. Add 2 ml of *chloroform* and shake; the *chloroform* layer becomes purple.

(C) It melts at about 135°, Appendix 5.11.

Specific optical rotation : Between −71° and −78°, determined in a 2.0 per cent w/v solution in *alcohol*, Appendix 5.12. Measure the angle of rotation 30 minutes after preparing the solution.

pH : Between 8.0 and 10.5, determined in a solution containing 0.1 g in 150 ml of *carbon dioxide-free water*, Appendix 5.10.

Heavy metals : Not more than 20 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

Sulphated ash : Not more than 0.2 per cent, Appendix 3.2.7.

Water : Not more than 10.0 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately about 25 mg and dissolve in 10 ml of *methyl alcohol*. Dilute to 100.0 ml with *water*. Carry out the *microbiological assay of antibiotics, Method A*, Appendix 4.1, and express the results in µg of Erythromycin per mg.

Storage : Store in well-closed, light-resistant containers at a temperature not exceeding 30°.

Labelling : The label on the container states (1) the date after which the contents are not intended to be used; (2) the storage conditions.

Erythromycin Tablets

Category : Antibacterial.

Dose : Erythromycin, 1 to 2 g daily, in divided doses.

Usual strength : 250 mg.

Standards : Erythromycin Tablets contain not less than 95.0 per cent and not more than 110.0 per cent of the stated amount of Erythromycin, $C_{37}H_{67}NO_{13}$. The tablets are enteric-coated.

Identification : Dissolve a quantity of the powdered tablets equivalent to 3 mg of Erythromycin as completely as possible in 2 ml of *acetone*; the solution complies with **Identification** test (B) described under Erythromycin.

Disintegration : Comply with the *disintegration test for enteric-coated tablets*, Appendix 5.6.1, operating the apparatus for one hour in *0.1N hydrochloric acid*.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

quantity of the powder equivalent to about 25 mg of Erythromycin and dissolve in 10 ml of *methyl alcohol*. Dilute to 100.0 ml with *water*. Carry out the *microbiological assay of antibiotics, Method A*, Appendix 4.1.

Storage : Store in tightly-closed containers at a temperature not exceeding 30°.

Labelling : The label on the container states (1) the date after which the tablets are not intended to be used; (2) the storage conditions.

Erythromycin Estolate

$C_{40}H_{71}NO_{14}, C_{12}H_{26}O_4S$ Mol. Wt. 1056.39

Category : Antibacterial.

Dose : The equivalent of 1 to 2 g of erythromycin daily, in divided doses for not more than ten days.

Description : White crystalline powder; odourless; tasteless.

Solubility : Practically insoluble in *water*; soluble in *alcohol* and in *chloroform*; insoluble in *dilute hydrochloric acid*.

Standards : Erythromycin Estolate is the 2-propionate dodecylsulphate of erythromycin, an antimicrobial substance produced by the growth of certain strains of *Streptomyces erythreus* Waksman. It contains not less than 600 µg of $C_{37}H_{67}NO_{13}$ per mg, calculated with reference to the anhydrous substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *erythromycin estolate R.S.*, Appendix 5.15 B.

(B) Carry out the method for *ascending paper chromatography*, Appendix 5.4.2, preparing a chromatogram, using as the mobile phase, *isobutyl methyl ketone* previously washed with *sodium bicarbonate solution* and then with *water*. Apply 3 µl of a 0.2 per cent w/v solution in *chloroform*. Elute until the solvent has travelled about 19 cm. Allow the paper to dry in air and place the portion containing the chromatogram in nutrient agar medium previously inoculated with *Bacillus pumilus* (N.C.T.C. No. 8241). After fifteen minutes, remove the paper and incubate the plate overnight. A clean zone of inhibition is produced near the position corresponding to the finishing line of the chromatogram but no zone half way down (distinction from erythromycin).

(C) Dissolve 15 mg in 2 ml of *acetone* and add 2 ml of *hydrochloric acid*; an orange-red colour is produced, which becomes red and finally deep purple. Add 2 ml of *chloroform* and shake; the chloroform layer becomes purple.

pH : Between 4.5 and 7.0, determined in an aqueous suspension containing 100 mg per ml, Appendix 5.10.

Acetone : Dissolve 0.1 g in 100 ml of *methyl alcohol* and to 1 ml of the resulting solution add 0.1 ml of *salicylaldehyde*, mix, add 1.5 ml of a saturated solution of *potassium hydroxide*, allow to stand for twenty minutes, and add 6 ml of *methyl alcohol*; the *extinction*, at 490 nm of a 1-cm layer of the resulting solution is not greater than the *extinction* obtained when 1 ml of a 0.002 per cent w/v solution of *acetone* in *methyl alcohol* is treated in a similar manner, Appendix 5.15 A.

Thiocyanate : Dissolve 0.1 g in *alcohol* and add 5 ml of a solution prepared by dissolving 3.35 g of *ferric chloride* in *water* and adding 52.5 ml of *nitric acid* and sufficient *water* to produce 200 ml. Dilute to 100 ml with *alcohol*; the *extinction*, at 470 nm of a 1-cm layer of the resulting solution is not greater than the *extinction* obtained when 2 ml of *potassium thiocyanate solution* containing 417 µg per ml is treated in a similar manner, Appendix 5.15 A.

Content of $C_{12}H_{26}O_4S$: Between 22.0 and 25.5 per cent, calculated with reference to the anhydrous substance, and determined by the following method. Weigh accurately about 0.56 g and dissolve in 5 ml of *dimethylformamide*; titrate with *0.1 N sodium methoxide*, using a 0.3 per cent w/v solution of *thymol blue* in *methyl alcohol* as indicator. Each ml of *0.1 N sodium methoxide* is equivalent to 0.02664 g of $C_{12}H_{26}O_4S$.

Undue toxicity : Complies with the test described under Bacitracin, using 0.5 ml of a suspension in a 10 per cent w/v solution of *Acacia*, containing the equivalent of 20 mg of erythromycin.

Water : Not more than 4.0 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately about 40 mg, dissolve in 40 ml of *methyl alcohol* and add 20 ml of *buffer solution, pH 7.0* and sufficient *water* to produce 100.0 ml. Maintain the solution at 60° for three hours, cool, and carry out the *microbiological assay of antibiotics, Method A*, Appendix 4.1. Express the results in µg of erythromycin per mg.

Storage : Store in well-closed, light-resistant container.

Labelling : The label on the container states (1) the date after which the contents are not intended to be used; (2) the storage conditions.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Erythromycin Estolate Tablets

Category : Antibacterial.

Dose : The equivalent of 1 to 2 g of erythromycin daily, in divided doses, for not more than ten days.

Usual strengths : 250 mg; 500 mg.

Standards : Erythromycin Estolate Tablets contain a quantity of Erythromycin Estolate equivalent to not less than 90.0 per cent and not more than 120.0 per cent of the stated amount of erythromycin. The tablets may be coated.

Identification : (A) Extract a quantity of the powdered tablets equivalent to 0.12 g of erythromycin with 100 ml of *chloroform* and filter. The filtrate complies with **Identification** test (B) described under Erythromycin Estolate.

(B) Comply with **Identification** test (C) described under Erythromycin Estolate, using a quantity of the powdered tablets equivalent to 10 mg of erythromycin.

Water : Not more than 7.0 per cent w/w, determined on the powdered tablets, Appendix 3.3.25.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of powder equivalent to about 0.25 g of erythromycin, dissolve in 400 ml of *methyl alcohol* and 200 ml of *buffer solution, pH 7.0* and sufficient *water for injection* to produce 1000.0 ml. Maintain the solution at 60° for three hours, cool, filter and carry out the *microbiological assay of antibiotics, Method A*, Appendix 4.1.

Storage : Store in tightly-closed containers.

Labelling : The label on the container states (1) the strength in terms of the equivalent amount of erythromycin; (2) (Film-coated) for tablets coated in this manner; (3) the date after which the tablets are not intended to be used; (4) the storage conditions.

Erythromycin Stearate

$C_{37}H_{67}NO_{13}, C_{18}H_{36}O_2$ Mol. Wt. 1018.42

Category : Antibacterial.

Dose : The equivalent of 1 to 2 g of erythromycin daily, in divided doses for not more than ten days.

Description : Colourless or slightly yellow crystals or white or slightly yellow powder; almost odourless; taste, slightly bitter.

Solubility : Practically insoluble in *water*, and in *acetone*; slightly soluble in *alcohol*, in *chloroform*, in *methyl alcohol* and in *solvent ether*.

Standards : Erythromycin Stearate is the stearate of Erythromycin, an antimicrobial substance produced by the growth of certain strains of *Streptomyces erythreus* Waksman, with stearic acid and sodium stearate. It contains not less than 550 µg of $C_{37}H_{67}NO_{13}$ per mg, calculated with reference to the anhydrous substance.

Identification : (A) To 5 mg add 2 ml of *sulphuric acid* and shake gently; a reddish brown colour is produced.

(B) Dissolve 3 mg in 2 ml of *acetone* and add 2 ml of *hydrochloric acid*; an orange colour is produced, which changes to red and then to deep purplish-red. Add 2 ml of *chloroform* and shake; the chloroform layer becomes purple.

(C) Heat gently 0.1 g with 5 ml of *dilute hydrochloric acid* and 10 ml of *water* until the solution boils; oily globules rise to the surface. Cool, remove the fatty layer, heat it with 3 ml of *0.1N sodium hydroxide*, and allow to cool; the solution sets to a gel; add 10 ml of hot *water* and shake, the solution froths. To 1 ml add *calcium chloride solution*; a granular precipitate insoluble in *hydrochloric acid* is produced.

pH : Between 6.0 and 11.0 determined in a 1 per cent suspension in *water*, Appendix 5.10.

Stearic acid : Between 5.0 and 18.5 per cent determined by the following method : Weigh accurately about 0.4 g and dissolve in 50 ml of *alcohol*, previously neutralised to *phenolphthalein solution* with *0.1N sodium hydroxide*. Titrate with *0.1N sodium hydroxide* to a pink end-point. Calculate the volume of *0.1N sodium hydroxide* required for each g of the substance and subtract the volume of *0.1N perchloric acid* required for each g of the substance in the test for **Erythromycin stearate**. Each ml of the difference is equivalent to 0.02845 g of stearic acid.

Sodium stearate : Not more than 6.0 per cent, determined by the following method: Moisten 2.0 g in a platinum dish with *sulphuric acid*, ignite gently, moisten again with *sulphuric acid*, ignite at about 800°, cool, and weigh. Each g of residue is equivalent to 4.317 g of sodium stearate.

Erythromycin stearate : Not less than 77.0 per cent of $C_{37}H_{67}NO_{13}, C_{18}H_{36}O_2$ calculated with reference to the anhydrous substance, when determined by the following method. Weigh accurately about 0.5 g and shake with 30 ml and three quantities, each of 25 ml, of *chloroform*, filtering each extract. Wash the filter with *chloroform* and evaporate the combined filtrate and washings on a water-bath to about 30 ml. Add 50 ml of *glacial acetic acid*, previously neutralised with *0.1N perchloric acid*, and two drops of *crystal-violet solution* and titrate with *0.1N perchloric acid* till the colour changes from violet to

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

green. Each ml of *0.1N perchloric acid* is equivalent to 0.1018 g of erythromycin stearate, $C_{37}H_{67}NO_{13},C_{18}H_{36}O_2$.

NOTE – The total of the percentages of stearic acid, sodium stearate and erythromycin stearate, all calculated with reference to the undried substance and water founded by the above methods must be not less than 98.0 per cent and not more than 103.0 per cent.

Undue toxicity : Complies with the test described under Bacitracin, Appendix 2.37 the dose being 0.5 ml of a suspension containing the equivalent of 80 mg of erythromycin per ml, prepared by grinding the sample in *water for injection* using one drop of *polysorbate 80* per g of sample.

Water : Not more than 4.0 per cent w/w, Appendix 3.3.25.

Assay : Carry out the *microbiological assay of antibiotics, Method A*, Appendix 4.1, using about 50 mg accurately weighed, dissolved in sufficient *methyl alcohol* to produce 100 ml. Express the result in µg of $C_{37}H_{67}NO_3$ per mg.

Storage : Store in well-closed, light-resistant containers.

Labelling : The label on the container states (1) the date after which the contents are not intended to be used; (2) the storage conditions.

Erythromycin Stearate Tablets

Category : Antibiotic.

Dose : The equivalent of 1 to 2 g of erythromycin daily, in divided doses.

Usual strengths : 100 mg; 250 mg.

Standards : Erythromycin Stearate Tablets contain not less than 90.0 per cent and not more than 120.0 per cent of the stated amount of erythromycin. The tablets are coated.

Identification : (A) To a quantity of the powdered tablets equivalent to about 3 mg of erythromycin, add 2 ml of *acetone* and 2 ml of *hydrochloric acid*; an orange colour is produced, which changes to red and then to purplish-red. Add 2 ml of *chloroform* and shake; the chloroform layer becomes purple.

(B) Extract a quantity of the powdered tablets equivalent to about 50 mg of erythromycin with 10 ml of *chloroform*, filter, and evaporate to dryness. The residue complies with **Identification** test (C) described under Erythromycin Stearate.

Loss on drying : Not more than 5.0 per cent, determined on 0.2 g of the powdered tablets by drying "in vacuo" for three hours, Appendix 5.8.

Disintegration : Maximum time, ninety minutes, Appendix 5.6.1.

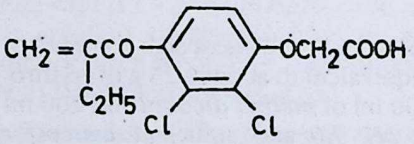
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 50 mg of erythromycin, dissolve in 200 ml of *methyl alcohol* and carry out the *microbiological assay of antibiotics, Method A*, Appendix 4.1.

Storage : Store in light-resistant containers.

Labelling : The label on the container states (1) the strength in terms of the equivalent amount of erythromycin; (2) the date after which the tablets are not intended to be used; (3) the storage conditions.

Ethacrynic Acid



$C_{13}H_{12}Cl_2O_4$ Mol. Wt. 303.14

Category : Diuretic.

Dose : 50 to 200 mg daily, in divided doses.

Description : White or almost white, crystalline powder; odourless or almost odourless.

Solubility : Very slightly soluble in *water*; freely soluble in *alcohol*, in *chloroform*, and in *solvent ether*.

Standards : Ethacrynic Acid is [2,3-dichloro-4-(2-ethylacryloyl)-phenoxy] acetic acid. It contains not less than 97.0 per cent and not more than the equivalent of 102.0 per cent of $C_{13}H_{12}Cl_2O_4$, calculated with reference to the dried substance.

Identification : (A) The light absorption, in the range 230 to 350 nm, of a 0.005 per cent w/v solution in a mixture of 1 volume of *N hydrochloric acid* and 99 volumes of *methyl alcohol* exhibits a well defined maximum only at 270 nm, Appendix 5.15 A.

(B) To 25 mg add 2 ml of *N sodium hydroxide* and heat for 5 minutes in a water-bath, cool, add 0.25 ml of *sulphuric acid (50 per cent v/v)*. Add 0.5 ml of a 10 per cent w/v solution of *chromotropic acid sodium salt* and,

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

cautiously 2 ml of *sulphuric acid*; a deep violet colour is produced.

(C) Burn 20 mg by the *oxygen-flask method*, Appendix 3.3.6, using 5 ml of *dilute sodium hydroxide solution* as the absorbing liquid. When the process is complete, acidify with *dilute sulphuric acid* and boil gently for two minutes; the solution gives the reaction of *chlorides*, Appendix 3.1.

Melting range : Between 121° to 125°, Appendix 5.11.

Light absorption : *Extinction* of a 1-cm layer of a 0.005 per cent w/v solution in a mixture of 1 volume of *N hydrochloric acid* and 99 volumes of *methyl alcohol* at the maximum at about 270 nm, 0.55 to 0.60, Appendix 5.15A.

Foreign substances : To 1.0 g in a glass-stoppered cylinder add 50 ml of an 8 per cent w/v solution of *sodium sulphite*, shake to dissolve, allow to stand for twenty minutes, and add 5 ml of *hydrochloric acid*. Transfer the solution in equal portions to two 50-ml plastic-stoppered centrifuge tubes and treat each portion in the following manner. Add 15 ml of *benzene* and shake vigorously, loosening the stopper once or twice to release the liberated sulphur dioxide. After shaking for two minutes, centrifuge, remove the upper layer, and repeat the extraction with two further quantitites, each of 15 ml of *benzene*. Combine the six extracts, evaporate to dryness on a water-bath, dry the residue at 60° at a pressure not exceeding 5 mm of mercury for two hours, cool, and weigh. The residue weighs not more than 20 mg.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying "in vacuo at 60°" for two hours, Appendix 5.8.

Assay : Weigh accurately about 0.2 g, dissolve in 40 ml of *glacial acetic acid* in a glass-stoppered flask, add 20 ml of *0.1N bromine* and 3 ml of *hydrochloric acid*, immediately stopper the flask, mix well, and allow to stand for one hour in the dark. Add 100 ml of *water* and 20 ml of *potassium iodide solution* and immediately titrate with *0.1N sodium thiosulphate*, using *starch solution*, added towards the end of the titration, as indicator. Repeat the operation without the ethacrynic acid; the difference between the titrations represents the amount of bromine required by the ethacrynic acid. Each ml of *0.1N bromine* is equivalent to 0.01516 g of $C_{13}H_{12}Cl_2O_4$.

Storage : Store in well-closed containers.

Ethacrynic Acid Tablets

Category : Diuretic.

Dose : Ethacrynic acid, 50 to 200 mg daily, in divided doses.

Usual strength : 50 mg.

Standards : Ethacrynic Acid Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Ethacrynic Acid, $C_{13}H_{12}Cl_2O_4$.

Identification : Mix a quantity of the powdered tablets equivalent to 50 mg of Ethacrynic Acid with *0.1N hydrochloric acid* and extract with two quantities, each of 40 ml of *methylene chloride*. Filter the extracts and add sufficient *methylene chloride* to produce 100 ml. Evaporate to dryness with the aid of gentle heat. The residue complies with **Identification** tests (A) and (B) described under Ethacrynic Acid.

Foreign substances : Moisten a quantity of the powdered tablets equivalent to 0.4 g of Ethacrynic Acid with 2 ml of *N hydrochloric acid*, allow to stand for fifteen minutes, add 25 ml of *light petroleum (boiling range, 60° to 80°)* and shake for two minutes. Centrifuge and discard the clear liquid. Add to the residue a further 25 ml of *light petroleum (boiling range, 60° to 80°)*, shake for two minutes, centrifuge, and again discard the clear liquid. Evaporate the remaining traces of light petroleum in a stream of *nitrogen*. Extract the residue with two quantities, each of 25 ml, of *methylene chloride* centrifuging to obtain a clear extract. Evaporate the combined extracts on a water-bath at 30° in a stream of *nitrogen* and complete the test described under Ethacrynic Acid, beginning at the words "add 50 ml .....".

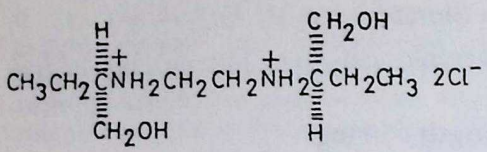
Other requirements : Comply with the requirements, under Tablets.

Assay : Weigh and powder 20 tablets. Add a quantity of the powder equivalent to 0.1 g of Ethacrynic Acid to 25 ml of *0.1N hydrochloric acid* and extract with two quantities, each of 50 ml, of *methylene chloride*. Filter the combined extracts and evaporate the filtrate to dryness with the aid of gentle heat. Dissolve the residue in 20 ml of *glacial acetic acid* in a glass-stoppered flask, add 10 ml of *0.1N bromine* and 3 ml of *hydrochloric acid*, immediately stopper the flask, mix well, and allow to stand for one hour. Add 50 ml of *water* and 10 ml of *potassium iodide solution* and immediately titrate with *0.1N sodium thiosulphate*, using *starch solution*, added towards the end of titration, as indicator. Repeat the operation using 20 ml of *glacial acetic acid* and beginning at the words "add 10 ml of *0.1N bromine*.....". The difference between the titrations represents the amount of bromine required by the ethacrynic acid. Each ml of *0.1N bromine* is equivalent to 0.01516 g of $C_{13}H_{12}Cl_2O_4$.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Ethambutol Hydrochloride



$C_{10}H_{24}N_2O_2$, 2HCl Mol. Wt. 277.23

Category : Antibacterial (tuberculostatic).

Dose : 15 mg to 25 mg per kg body weight daily, for two months, followed by 25 mg per kg body weight daily.

Description : White crystalline powder, almost odourless.

Solubility : Soluble in *water* and in *alcohol*; slightly soluble in *chloroform* and in *solvent ether*.

Standards : Ethambutol Hydrochloride is (*R*, *R*)-*N*, *N'*-bis-(1-hydroxymethylpropyl) ethylenediammonium dichloride. It contains not less than 98.0 per cent of $C_{10}H_{24}N_2O_2$, 2HCl, calculated with reference to the dried substance.

Identification : (A) : The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to those in the spectrum of *ethambutol hydrochloride R.S.*, Appendix 5.15 B.

(B) Dissolve 0.1 g in 10 ml of *water*, add 2 ml of 1 per cent w/v solution of *copper sulphate*, followed by 1 ml of *N sodium hydroxide*; a distinct blue colour is produced.

(C) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

Melting range : Between 199° and 204°, Appendix 5.11.

Specific optical rotation : Between +6.0° and +6.6°, determined in a 10 per cent w/v solution in *water*, Appendix 5.12.

Heavy metals : Not more than 20 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

(+)-2-Aminobutan-1-ol : Not more than 1.0 per cent, determined by the following method: Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 11 volumes of *ethyl acetate*, 7 volumes of *glacial acetic acid*, 1 volume of *hydrochloric acid*, and 1 volume of *water* as the mobile phase. Apply separately to the plate 2 µl of each of two solutions in *methyl alcohol* containing (1) 5.0 per cent w/v of the substance being examined and (2) 0.050 per cent w/v of (+)-*2-aminobutan-1-ol*. After removal of the plate, allow it to dry in air, heat at 105° for five minutes, cool, spray with *cadmium* and *ninhydrin solution* and heat at 90° for five minutes. The spot in the chromatogram obtained with solution (2) is more intense than any corresponding spot in the chromatogram obtained with solution (1).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying at 105° for 2 hours, Appendix 5.8.

Assay : Weigh accurately about 0.2 g and dissolve in 10 ml of *2N sodium hydroxide*, and extract with five quantities, each of 25 ml, of *chloroform*, filtering each extract through a layer of *anhydrous sodium sulphate*, evaporate the combined filtrates just to dryness in a current of air, dissolve the residue in 100 ml of *glacial acetic acid*. Add two drops of *crystal-violet solution* and titrate with *0.1N perchloric acid*. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.01386 g of $C_{10}H_{24}N_2O_2$,2HCl.

Storage : Store in well-closed containers.

Ethambutol Tablets

Category : Antibacterial (tuberculostatic)

Dose : Ethambutol Hydrochloride, 15 to 25 mg per kg body weight, daily.

Usual strengths : 200 mg; 400 mg.

Standards : Ethambutol Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Ethambutol Hydrochloride, $C_{10}H_{24}N_2O_2$, 2HCl. The tablets may be coated.

Identification : (A) Shake a quantity of the powdered tablets, equivalent to about 0.1 g of Ethambutol Hydrochloride, with 10 ml of *water*, filter, and to the filtrate add 2 ml of a 1.0 per cent w/v solution of *copper sulphate* followed by 1 ml of *N sodium hydroxide*; a distinct blue colour is produced.

(B) Extract a quantity of the powdered tablets equivalent to 50 mg of Ethambutol Hydrochloride with 5 ml of *methyl alcohol*, filter and evaporate the filtrate to dryness. The *infra-red absorption spectrum* of the residue exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *ethambutol hydrochloride R.S.*, Appendix 5.15 B.

(+)-2-Aminobutan-1-ol : Carry out the test described under Ethambutol Hydrochloride. For solution (1) shake a quantity of the powdered tablets equivalent to 0.5 g of Ethambutol Hydrochloride for five minutes with sufficient *methyl alcohol* to produce 10 ml and filter.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.2 g of

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Ethambutol Hydrochloride, mix with 10 ml of *2N sodium hydroxide* and extract with five quantities each of 25 ml. of *chloroform* filtering each extract through a layer of *anhydrous sodium sulphate*; evaporate the combined extracts almost to dryness, dissolve the residue in 100 ml of *glacial acetic acid*; add two drops of *crystal-violet solution* and titrate with *0.1N perchloric acid*. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.01386 g of $C_{10}H_{24}N_2O_2$, 2HCl.

Storage : Store in well-closed containers.

Anaesthetic Ether

$(CH_3CH_2)_2O$

$C_4H_{10}O$ Mol. Wt. 74.12

Category : General anaesthetic.

Description : Clear, colourless liquid; volatile; very mobile; characteristic odour and burning taste; highly flammable.

Solubility : Soluble in *water*, miscible with *alcohol*, with *chloroform*, with *benzene* and with fixed and volatile oils.

Standards : Anaesthetic Ether is diethyl ether containing a suitable non-volatile stabiliser in a proportion not greater than 0.002 per cent w/v.

Boiling range : Between 34° and 36°, Appendix 5.3.

CAUTION—It is dangerous to determine the boiling range, if the sample does not comply with the test for peroxides.

Specific gravity : Between 0.713 and 0.716, Appendix 5.19.

Acidity : To 20 ml of *alcohol* add five drops of *bromothymol blue solution* and add dropwise *0.02N sodium hydroxide* until the blue colour persists for 30 seconds. Add 25 ml of the substance to be examined, shake and again add dropwise *0.02N sodium hydroxide* until the blue colour appears and persists for 30 seconds. Not more than 0.4 ml of *0.02N sodium hydroxide* is required.

Peroxides : Place 8 ml of *potassium iodide and starch solution* in a 12-ml glass-stoppered cylinder of about 1.5 cm diameter. Fill completely with the substance to be examined, insert the stopper, shake vigorously and allow to stand in the dark for 30 minutes. No colouration is produced.

Acetone and aldehyde : Place 2 ml of *alkaline potassium mercuri-iodide solution* in a 12-ml glass-stoppered cylinder of about 1.5 cm diameter and fill completely with the substance to be examined, insert the stopper and shake vigorously for 15 seconds and set aside for five minutes. No colour or turbidity, except for slight opalescence, is produced.

If the ether does not comply with the test, distil 40 ml *(after ensuring that it complies with the test for peroxides)* until only 5 ml remains, and repeat the test using 10 ml of the distillate.

Foreign odour : Pour 10 ml in successive portions on to a clean filter paper and allow to evaporate spontaneously; no foreign odour is detectable at any stage of evaporation.

Non-volatile matter : Evaporate 50 ml on a water-bath and dry at 100° to 105° *(after ensuring that the sample complies with the test for peroxides)*. The residue weighs not more than 1.5 mg.

Methyl alcohol : To 10 ml, add 5 ml of *alcohol (20 per cent)* and 5 ml of *water*, in a separator, shake vigorously, set aside and allow the mixture to separate and draw off the lower layer. To 5 ml of the lower layer add 2.0 ml of *potassium permanganate and phosphoric acid solution*, set aside for 10 minutes and add 2.0 ml of *oxalic acid* and *sulphuric acid solution* and 5 ml of *decolourised magenta solution*. Set aside for 30 minutes; no colour is produced.

Storage : Store in well-closed, light-resistant containers in a cool place. Ether remaining in a partly used container may deteriorate rapidly.

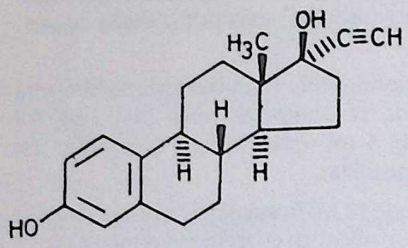
Labelling : The label on the container states (1) "Very flammable. Do not use near a naked flame"; (2) The name and proportion of any stabiliser added.

NOTE—It is absolutely essential that a preservative of the type of sodium pyrogallate, hydroquinone, or propyl gallate in suitable concentrations shall be added in Anaesthetic Ether intended for use in tropical climates unless the Anaesthetic Ether is stored in a copper container or in a container copper-plated internally. The preservative used and its concentration shall be declared on the label.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Ethinylestradiol



$C_{20}H_{24}O_2$ Mol. Wt. 296.41

Dose : In the treatment of menopausal symptoms, 10 to 50 µg daily. For the suppression of lactation, 0.1 mg thrice daily for three days followed by 0.1 mg daily for six days. In the treatment of Carcinoma of the prostate, 0.1 to 1 mg, daily.

Description : White or slightly cream coloured crystalline powder; odourless.

Solubility : Practically insoluble in *water*; soluble in *alcohol*, in *chloroform*, in *solvent ether*, in *acetone*, in vegetable oils, and in solutions of alkali hydroxides.

Standards : Ethinylestradiol is 19-nor-17*α*-pregna-1, 3, 5(10) trien-20-yne-3, 17*β*-diol. It contains not less than 97.0 per cent and not more than the equivalent of 102.0 per cent of $C_{20}H_{24}O_2$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as and have similar relative intensities to, those in the spectrum of *ethinylestradiol R.S.*, Appendix 5.15 B.

(B) Dissolve about 2 mg in 2 ml of *sulphuric acid*; the solution is orange-red by transmitted light and shows a yellow-green fluorescence in reflected light.

(C) To 1 ml of the above solution add one drop of *ferric ammonium sulphate solution* and 2 ml of *water*; a reddish-brown flocculant precipitate is formed.

(D) Dissolve about 25 mg in 10 ml of a 5 per cent w/v solution of *potassium hydroxide* contained in a glass-stoppered tube, add 0.1 g of *benzoyl chloride*; a precipitate is produced; recrystallise the precipitate from *methyl alcohol* and dry; the crystals melt between 200° and 202°, Appendix 5.11.

Melting range : Between 182° and 184°, Appendix 5.11, it may also occur in a form which melts between 141° and 146° due to polymorphism.

Clarity of solution : A 5 per cent w/v solution in *alcohol* is clear.

Specific optical rotation : Between 0° and +5°, determined in a 5.00 per cent w/v solution in *dioxan*, Appendix 5.12.

Light absorption : The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.01 per cent w/v solution in *ethyl alcohol*, exhibits a maximum at about 281 nm, Appendix 5.15 A, *extinction* at 281 nm, between 0.69 and 0.72.

Oestione : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 92 volumes of *ethylene chloride* and 8 volumes of *methyl alcohol* and 0.1 volume of *water* as the mobile phase. Apply separately to plate 5µl of each of two solutions containing (1) 0.2 g of the substance being examined dissolved in a mixture of 9 volumes of *chloroform* and 1 volume of *methyl alcohol* and diluted to 100.0 ml with the same mixture and (2) 0.02 per cent w/v of *oestione R.S.* in a mixture of 9 volumes of *chloroform*, one volume of *methyl alcohol*. After removing the plate, allow it to dry in air and then heat at 110° for ten minutes. Spray with a 10 per cent w/v solution of *sulphuric acid* in *alcohol* and again heat at 110° for ten minutes. Examine under ultra-violet lamp, having a maximum output at about 365 nm. Any spot in the chromatogram obtained with solution (1) is less intense than the corresponding fluorescent spot in the chromatogram obtained with solution (2).

Sulphated ash : Not more than 0.5 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.200 g and dissolve in 40 ml of *tetrahydrofuran*, add 10 ml of 10 per cent w/v solution of *silver nitrate* and titrate with *0.1N sodium hydroxide*, determining the end-point potentiometrically. Each ml of *0.1N sodium hydroxide* is equivalent to 0.02964 g of $C_{20}H_{24}O_2$.

Storage : Store in well-closed, light-resistant containers.

Ethinylestradiol Tablets

Category : Estrogen.

Dose : Ethinylestradiol. In the treatment of menopausal symptoms, 10 to 50 µg daily. For the suppression of lactation, 100 µg thrice daily for three days, followed by 100 µg daily for six days. In the treatment of carcinoma of the prostate and mammary carcinoma, 0.1 to 1 mg daily.

Usual strength : 20 µg.

Standards : Ethinylestradiol Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Ethinylestradiol, $C_{20}H_{24}O_2$.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Identification : Triturate a quantity of the powdered tablets equivalent to 100 µg of Ethinylestradiol with 0.5 ml of *0.1 N sodium hydroxide* and 5 ml of *water*, allow to stand for five minutes, filter, acidify the filtrate with 3 drops of *sulphuric acid*, add 3 ml of *solvent ether*, shake and allow to separate. Evaporate the ether layer to dryness and heat the residue on a water-bath for five minutes with 0.2 ml of *glacial acetic acid* and 2 ml of *phosphoric acid*; a pink colour with an intense orange fluorescence is produced.

Uniformity of content : Powder one tablet and triturate with successive quantities, each of 5 ml, of warm *methyl alcohol*. Filter the extracts through the plug of cotton wool into a small beaker. Wash the filter with a small quantity of *methyl alcohol* and add the washings to the main extracts. Evaporate to dryness on a water-bath with the aid of a current of *nitrogen*. Complete the **Assay** beginning at the words ".... and transfer the residue to a separator.....". Calculate the content of $C_{20}H_{24}O_2$ in the tablet. Repeat the operation with a further nine tablets and calculate the content of the ten tablets. The content of each tablet is between 80 per cent of 120 per cent of the average, except that for one tablet the content may be between 75 and 125 per cent of the average.

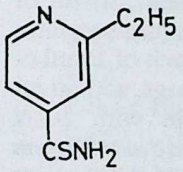
Other requirements : Comply with the requirements stated under Tablets.

NOTE – Use completely dry glassware and separators fitted with solvent resistant stopcocks and use iso-octane that gives no colour, when shaken with an equal volume of sulphuric acid.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of powder equivalent to 150 µg of Ethinylestradiol, add 5 ml of *water* and heat on a water-bath for five minutes with occasional stirring. To the warm mixture add 70 ml of *methyl alcohol* and shake for ten minutes. Filter the mixture into a 100-ml volumetric flask, wash the flask and filter with a small quantity of *methyl alcohol*. Dilute the filtrate and washings to volume with *methyl alcohol* and mix. Evaporate 10.0 ml to dryness on a water-bath with the aid of a current of *nitrogen* and transfer the residue to a separator with successive quantities, each of 1 ml, of *N sodium hydroxide*. Rinse with 2 ml of *dilute sulphuric acid* and add the washings to a separator. Extract with three successive quantities, each of 25 ml, of a mixture of 1 volume of *chloroform* and 49 volumes of *iso-octane*, extracting each time for two minutes. Combine the solvent extracts in a second separator through a plug of cotton wool and wash the filter with 5 ml of *iso-octane*. Add 5.0 ml of *sulphuric acid* in *methyl alcohol* from a pipette and allow to drain for not less than two minutes. Shake for two minutes, allow to separate completely and transfer 4.0 ml of the fluorescent pink phase to a glass-stoppered centrifuge tube containing 0.5 ml of *methyl alcohol*. Mix vigorously and centrifuge. Measure the *extinction* of 1-cm layer of the resulting solution at the maximum at about 538 nm, Appendix 5.15 A. Calculate the content of $C_{20}H_{24}O_2$, from the extinction obtained from a solution treated in the following manner: Weigh accurately about 30 mg of *ethinylestradiol R.S.* and dissolve in sufficient *methyl alcohol* to produde 50.0 ml. Dilute 5.0 ml to 100.0 ml with *iso-octane*. Dilute 5.0 ml of the resulting solution to 50.0 ml with *iso-octane* and mix. Pipette 5.0 ml into a separator, add 75 ml of a mixture of one volume of *chloroform* and 49 volumes of *iso-octane*. Complete the **Assay** beginning at the words "Add 5.0 ml of *sulphuric acid in methyl alcohol...*".

Storage : Store in well-closed, light-resistant containers.

Ethionamide



$C_8H_{10}N_2S$ Mol. Wt. 166.24

Category : Antibacterial (tuberculostatic).

Dose : 0.5 to 1 g daily, in divided doses.

Description : Bright yellow, crystalline powder; odour, slight; taste, unpleasant and sulphurous.

Solubility : Insoluble in *water*; soluble in *alcohol*; slightly soluble in *solvent ether*, and in *chloroform*.

Standards : Ethionamide is 2-ethyl-4-pyridinecarbothioamide. It contains not less than 98.5 per cent of $C_8H_{10}N_2S$, calculated with reference to the dried substance.

Identification : (A) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.001 per cent w/v solution in *alcohol* exhibits a maximum only at 290 nm; *extinction* at 290 nm, about 0.42, Appendix 5.15 A.

(B) Heat 0.1 g with 5 ml of *sodium hydroxide solution*; the vapours evolved turn *red litmus paper* blue.

(C) Heat 0.1 g with 5 ml of *N hydrochloric acid*; the vapours evolved blacken *lead acetate paper*.

Melting range : Between 158° and 165°, Appendix 5.11.

pH : Between 6.0 and 7.0 in a 1 in 100 slurry in *water*, Appendix 5.10.

Heavy metals : Not more than 10 parts per million, determined on 2.0 g by Method B, Appendix 3.2.4.

Foreign substances : Carry out in subdued light, the method for *thin-layer chromatography*, Appendix 5.4.3,

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

using *silica gel GF 254*, as the coating substance. Use as the mobile phase, a mixture of 9 volumes of *chloroform* and 1 volume of *methyl alcohol*. Apply separately to the plate 10 µl each of two solutions, freshly prepared in *methyl alcohol* containing (1) 5.0 per cent w/v of the substance being examined and (2) 0.025 per cent w/v of the substance being examined. After removal of the plate, allow it to dry in air, and examine under an ultraviolet lamp having a maximum output at about 254 nm. Any spot in the chromatogram obtained with solution (1) other than the principal spot is not more intense than the spot in the chromatogram obtained with solution (2).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 2.0 per cent determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.3 g and dissolve in 10 ml of *dilute sulphuric acid*. Add 100 ml of *water*, 20 ml of *dilute ammonia solution* and immediately, 50 ml of *0.1N silver nitrate*. Allow to stand for a few minutes, filter and wash the filter with three quantities, each of 10 ml of *water*. To the combined filtrate and washings, add 60 ml of *dilute nitric acid*, cool, and titrate with *0.1N ammonium thiocyanate*, using 5 ml of *ferric ammonium sulphate solution* as indicator. Each ml of *0.1N silver nitrate* is equivalent to 0.008312 g of $C_8H_{10}N_2S$.

Storage : Store in tightly-closed, light-resistant containers, in a cool place.

Ethionamide Tablets

Category : Antibacterial (tuberculostatic).

Dose : Ethionamide, 0.5 to 1 g daily, in divided doses.

Usual strength : 125 mg.

Standards : Ethionamide Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Ethionamide, $C_8H_{10}N_2S$. The tablets may be coated.

Identification : (A) Shake a quantity of the powdered tablets equivalent to 0.1 g of Ethionamide with 80 ml of *alcohol*, filter, and add sufficient *alcohol* to produce 100 ml, dilute 1 ml to 100 ml with *alcohol*; the light absorption of the resulting solution, in the range of 230 to 350 nm, exhibits a maximum only at 290 nm, *extinction* at 290 nm, of 1-cm layer, about 0.42, Appendix 5.15A.

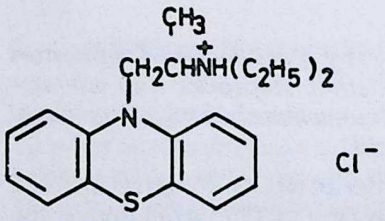
(B) Comply with **Identification** tests (B) and (C) described under Ethionamide.

Foreign substances : Comply with the test described under Ethionamide, using as solution (1) a solution prepared in the following manner: Shake a quantity of the powdered tablets equivalent to 0.75 g of Ethionamide with 20 ml of *methyl alcohol*, add sufficient *methyl alcohol* to produce 25 ml, centrifuge, and use the supernatant liquid.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Stir a quantity of the powder equivalent to 0.25 g of Ethionamide with 20 ml of *glacial acetic acid* for two minutes in a sintered-glass filter, filter, repeat the extraction with three quantities, each of 20 ml, of *glacial acetic acid*, and wash the filter with 20 ml of *glacial acetic acid*. To the combined filtrate and washings add 0.5 ml of *acetic anhydride* and titrate with *0.1N perchloric acid*, determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.01662 g of $C_8H_{10}N_2S$.

Ethopropazine Hydrochloride



$C_{19}H_{24}N_2S, HCl$ Mol. Wt. 348.93

Category : Antiparkinsonian.

Dose : Initial, 50 mg daily; subsequent doses increasing gradually to 500 mg daily; in divided doses.

Description : White or slightly creamy white, crystalline powder; almost odourless; taste, bitter.

Solubility : Slightly soluble in *water*; sparingly soluble in *alcohol*; freely soluble in *chloroform*; insoluble in *solvent ether*.

Standards : Ethopropazine Hydrochloride is *N,N*-diethyl-3-(10-phenothiazinyl)prop-2-yl-ammonium chloride. It contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of $C_{19}H_{24}N_2S, HCl$, calculated with reference to the dried substance.

Identification : (A) The light absorption in the range 230 to 350 nm of a 1-cm layer of a 0.0005 per cent w/v solution in *alcohol* exhibits a maximum at 252 nm, and a less well defined maximum at about 303 nm; *extinction* at 252 nm, about 0.42, Appendix 5.15A.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

(B) Complies with **Identification** test (D) described under Chlorpromazine Hydrochloride, using *ethopropazine hydrochloride R.S.*, instead of *chlorpromazine hydrochloride R.S.*

(C) Dissolve 5 mg in 2 ml of *sulphuric acid*, and allow to stand for five minutes, a red colour is produced.

(D) A solution (1 in 10) gives the reactions of *chlorides* Appendix 3.1.

Acidity or Alkalinity : Dissolve 0.15 g in 50 ml of *carbon dioxide-free water*; the solution is not acid to *methyl red solution*, and requires not more than 0.2 ml of *0.01N hydrochloric acid* for neutralisation.

Heavy metals : Not more than 20 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

Foreign substances : Carry out the method for *thin-layer chromatography* as in **Identification** test (B) using for solution (2) 0.005 per cent of the substance being examined. Any spot in the chromatogram obtained with solution (1), other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (2).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.7 g, dissolve in 200 ml of *acetone*, add 15 ml of *mercuric acetate solution*, and titrate with *0.1N perchloric acid* using 3 ml of a saturated solution of *methyl orange* in *acetone* as indicator. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.03489 g of $C_{19}H_{24}N_2S$, HCl.

Storage : Store in well-closed, light-resistant containers.

Ethopropazine Tablets

Category : Antiparkinsonian.

Dose : Ethopropazine Hydrochloride. Initial dose 50 mg daily; subsequent doses increasing gradually to 500 mg daily, in divided doses.

Usual strength : 50 mg.

Standards : Ethopropazine Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Ethopropazine Hydrochloride, $C_{19}H_{24}N_2S$, HCl. The tablets may be coated.

Identification : (A) Comply with **Identification** test (B) described under Ethopropazine Hydrochloride, applying to the plate 2 µl of each of the following solutions. For solution (1) shake a quantity of the powdered tablets with sufficient *chloroform* to produce a solution containing the equivalent of 2 mg of Ethopropazine Hydrochloride per ml; centrifuge and use the supernatant liquid; solution (2) is a 0.2 per cent w/v solution of *ethopropazine hydrochloride R.S.* in *chloroform.*

(B) To a quantity of the powdered tablets equivalent to 5 mg of Ethopropazine Hydrochloride add 5 ml of *sulphuric acid* and allow to stand for five minutes, a red colour is produced.

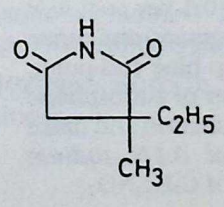
(C) Stir a quantity of the powdered tablets equivalent to 0.2 g of Ethopropazine Hydrochloride with 10 ml of warm *chloroform* for five minutes, filter, shake the filtrate with a mixture of 1 ml of *N sodium hydroxide* and 5 ml of *water*, allow to separate, wash the chloroform-layer with 5 ml of *water*, and evaporate to dryness. Dissolve the residue in 2 ml of *methyl alcohol*, pour into a solution of 0.5 g of *picric acid* in 10 ml of *methyl alcohol*, previously warmed to 50°, and filter; melting point of the residue, after washing with *methyl alcohol*, about 145°, Appendix 5.11.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Protect the solutions from light throughout the assay. Weigh and powder 20 tablets. Extract a quantity of the powder equivalent to 50 mg of Ethopropazine Hydrochloride with four quantities, each of 20 ml, of *alcohol.* Filter, dilute the filtrate to 100.0 ml with *alcohol*, dilute 10.0 ml to 100.0 ml with *alcohol* and dilute 10.0 ml of the dilution to 100.0 ml with *alcohol.* Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 252 nm, Appendix 5.15 A. Calculate the content of $C_{19}H_{24}N_2S$, HCl, taking 845 as the value of E(1 per cent, 1-cm) at the maximum at about 252 nm.

Storage : Store in tightly-closed containers.

Ethosuximide



$C_7H_{11}NO_2$ Mol. Wt. 141.17

Category : Anticonvulsant.

Dose : 500 mg daily, in divided doses increasing to 2 g, as necessary.

Description : White or almost white powder or waxy solid; odourless or almost odourless; taste, slightly bitter.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Solubility : Freely soluble in *water*, in *chloroform*, in *alcohol*, and in *solvent ether*; slightly soluble in *light petroleum*.

Standards : Ethosuximide is 2-ethyl-2-methylsuccinimide. It contains not less than 98.0 per cent of $C_7H_{11}NO_2$, calculated with reference to the anhydrous substance.

Identification : (A) The *infra-red absorption spectrum* of a molten film exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *ethosuximide R.S.*, Appendix 5.15 B.

(B) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of 0.05 per cent w/v solution in *alcohol* exhibits a maximum only at 248 nm; *extinction* at 248 nm, about 0.43, Appendix 5.15A.

(C) Heat 0.1 g with 0.2 g of *resorcinol*, and two drops of *sulphuric acid* at 140° for five minutes, add 5 ml of *water*, make alkaline with *sodium hydroxide solution*, and pour a few drops into a large volume of *water*; a bright green fluorescence is obtained.

Melting range : Between 45° and 52° Appendix 5.11.

Acidic substances : Dissolve 5.0 g in 50 ml of *water* by warming on a water-bath for five minutes. Cool, and titrate with *0.1N sodium hydroxide*, using *bromocresol green solution* as indicator; not more than 0.7 ml is required.

Cyanide : Dissolve 1 g in 10 ml of *alcohol*, add 3 drops of *ferrous sulphate solution*, 1 ml of *N sodium hydroxide*, and a few drops of *ferric chloride test-solution*. Warm gently, and acidify with *dilute sulphuric acid*, no blue precipitate or blue colour is formed within fifteen minutes.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Water : Not more than 0.5 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately about 0.2 g, dissolve in 50 ml of *dimethyl formamide*, add 2 drops of a 0.1 per cent w/v solution of *azo-violet* in *dimethyl formamide*, and titrate with *0.1N sodium methoxide* to a deep blue end-point, taking precautions to prevent absorption of atmospheric carbon dioxide. Perform a blank determination and make any necessary correction. Each ml of *0.1N sodium methoxide* is equivalent to 0.01412 g of $C_7H_{11}NO_2$.

Storage : Store in well-closed containers.

Ethyl Chloride

C_2H_5Cl Mol. Wt. 64.51

Category : Anaesthetic.

Description : Gaseous at ordinary temperatures and pressures but is generally compressed to a colourless, mobile, flammable and very volatile liquid; odour, pleasant and ethereal.

Solubility : Slightly soluble in *water* ; miscible with *alcohol* and with *solvent ether*.

Identification : (A) It burns with a luminous flame with the production of hydrogen chloride.

(B) Hydrolyse a few ml with *5N sodium hydroxide*; the resulting solution gives the reaction of *chlorides*, and, after the addition of *iodine solution* and warming, crystals of iodoform, Appendix 3.1.

Acidity or Alkalinity; Ionisable chlorides and Ethyl alcohol : Shake 10 ml with 10 ml of ice-cold *water* and allow the ethyl chloride to evaporate at room temperature; the residual liquid complies with the following: (1) It is neutral to *litmus solution*; (2) 5 ml gives no turbidity with *silver nitrate solution*; (3) Warm 5 ml with *iodine solution* and *sodium carbonate*; no iodoform is produced.

Distillation range : Into a dry 100-ml measuring cylinder insert a stopper carrying a short exit tube not less than 6 mm in internal diameter and an accurately standardised short-bulb thermometer covering the range −20° to +30° and graduated in tenths of a degree. Cover the bulb of the thermometer with a piece of very fine muslin, free from grease and sizing materials, so that one end hangs down about 10 mm below the bulb. Cool the cylinder in ice-water, transfer to it 100 ml of the sample, previously cooled in ice-water, insert the stopper, and adjust the thermometer so that the end of the muslin dips into the liquid and the bulb is above the surface. Replace the ice-water with water between 20° and 26° and observe the temperature when 5 ml of sample has evaporated and again when 5 ml remains. Continually lower the thermometer to maintain its position relative to the liquid surface throughout the test. Correct the observed temperature by adding 0.35° per 10 torr that the barometric pressure is below 760 torr or by subtracting 0.35° per 10 torr above. The corrected temperatures are not lower than 12.0° and not higher than 12.5°.

Other organic compounds : On evaporation, no foreign odour is detectable.

Non-volatile matter : Not more than 0.01 per cent w/w, when evaporated and dried at 105°.

Storage : Store at a temperature below 15° and protect from light.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Ethyl Oleate

$HC(CH_2)_7COOC_2H_5$
$\|$
$HC(CH_2)_7CH_3$

$C_{20}H_{38}O_2$ Mol. Wt. 310.52

Category : Pharmaceutical aid.

Description : Pale-yellow oil; odour and taste, strong and disagreeable.

Solubility : Insoluble in *water*, miscible with *alcohol*, with *chloroform*, with *solvent ether* and with fixed oils.

Standards : Ethyl Oleate is ethyl (Z)-9-octadecenoate. It contains not less than 98.0 per cent w/w and not more than the equivalent of 105.0 per cent w/w of the esters of oleic and related acids, calculated as $C_{20}H_{38}O_2$.

Acid value : Not more than 0.5, Appendix 3.3.15.

Iodine value : Between 75 and 85, Appendix 3.3.18.

Wt. per ml : Between 0.869 g and 0.874 g determined at 20°, Appendix 5.19.

Peroxides : Dissolve 5.0 g in 15 ml of *chloroform*, add 20 ml of *glacial acetic acid* and 0.5 ml of a saturated solution of *potassium iodide*, mix and allow to stand for exactly one minute in the dark. Add 30 ml of *water*, and titrate with *0.01N sodium thiosulphate*, using *starch solution* as indicator. Not more than 2.5 ml of *0.01N sodium thiosulphate* is required.

Assay : Carry out the method for the *determination of esters*, Appendix 3.3.2, continuing the boiling for two hours over a flame. Each ml of *0.5N alcoholic potassium hydroxide* is equivalent to 0.1553 g of $C_{20}H_{38}O_2$.

Storage : Store in well-closed, well-filled container, or in an atmosphere of nitrogen and protected from light.

Ethylenediamine Hydrate

$H_2NCH_2CH_2NH_2, H_2O$

$C_2H_8N_2, H_2O$ Mol. Wt. 78.11

Category : Pharmaceutical aid (for Aminophylline Injection).

Description : Clear, colourless or slightly yellow liquid; odour, ammoniacal.

Solubility : Miscible with *water* and with *alcohol*; slightly soluble in *chloroform* and in *solvent ether*.

Standards : Ethylenediamine Hydrate is the monohydrate of 1,2-ethanediamine. It contains not less than 97.5 per cent and not more than the equivalent of 101.5 per cent of $C_2H_8N_2, H_2O$.

Identification : (A) Dilute 1 ml to 6 ml with *water*. To 3 drops of the solution add 2 ml of a 1 per cent w/v solution of *copper sulphate*, and shake; a purple-blue colour is produced.

(B) It is strongly alkaline.

Ammonia and other bases : Weigh accurately about 1.5 ml and transfer with the aid of *alcohol* to a small dish. Add, with stirring, 20 ml of *dilute hydrochloric acid*, rinse the rod with 5 ml of *alcohol*, and evaporate the solution on a water-bath to dryness, then dry at 105° for one hour. Each g of residue is equivalent to 0.5872 g of $C_2H_8N_2, H_2O$. Calculate the percentage of $C_2H_8N_2, H_2O$; the result is within 0.5 per cent above or below the percentage of ethylenediamine found by the **Assay.**

Heavy metals : Not more than 20 parts per million, determined by Method A, Appendix 3.2.4, on a solution, prepared in the following manner: Evaporate 5 ml on a water-bath to dryness, add to the residue 1 ml of *hydrochloric acid* and 0.5 ml of *nitric acid* and evaporate to dryness. Dissolve the residue in 20 ml of warm *water*, cool, add sufficient *water* to produce 100 ml, mix, and use 20 ml of the resulting solution for the test.

Iron : To the residue obtained in the test for **Non-volatile matter**, add 1 ml of *hydrochloric acid* and 0.5 ml of *nitric acid*, and evaporate to dryness on a water-bath. Dissolve the residue in 20 ml of warm *water* and dilute with *water* to 100 ml. 40 ml of the solution complies with the *limit test for iron*, Appendix 3.2.5.

Non-volatile matter : Not more than 0.02 per cent w/v, determined on 5.0 ml by evaporating to dryness on a water-bath and drying at 105° for one hour.

Assay : Weigh accurately about 1.5 g, dissolve in 75 ml of *water* and titrate with *N hydrochloric acid*, using *bromophenol blue solution* as indicator, until a yellow colour is produced. Each ml of *N hydrochloric acid* is equivalent to 0.03906 g of $C_2H_8N_2, H_2O$.

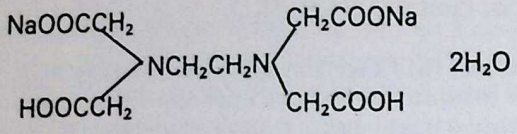
Storage : Store in well-closed, light-resistant containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Edetate Disodium

Disodium Edetate



$C_{10}H_{14}N_2Na_2O_8, 2H_2O$ Mol.Wt. 372.24

Category : Pharmaceutical aid (Chelating agent).

Description : White, crystalline powder; odourless; taste, slightly bitter.

Solubility : Soluble in *water*; slightly soluble in *alcohol*; insoluble in *chloroform* and in *solvent ether.*

Standards : Edetate Disodium is the dihydrate of disodium ethylenediamine-*N*,*N*,*N*′,*N*′-tetraacetate. It contains not less than 98.0 per cent of $C_{10}H_{14}N_2Na_2O_8, 2H_2O$.

Identification : (A) Dissolve 0.5 g in 10 ml of *water*, add 0.5 ml of *calcium chloride solution*, make alkaline to *litmus paper* with *dilute ammonia solution* and add 5 ml of *ammonium oxalate solution*; no precipitate is produced.

(B) Dissolve 2 g in 25 ml of *water*; add 2 ml of a 10 per cent w/v solution of *lead nitrate*, shake, and add 5 ml of *potassium iodide solution*; no yellow precipitate is formed. Make alkaline to *litmus paper* with *dilute ammonia solution*, and add 5 ml of *ammonium oxalate solution*; no precipitate is formed.

(C) Ignite; the residue gives the reactions of *sodium*, Appendix 3.1.

pH : Between 4.0 and 6.0, determined in 5.0 per cent w/v solution, Appendix 5.10.

Iron : 0.5 g complies with the *limit test for iron*, Appendix 3.2.5, 1.0 g of *calcium chloride* being added to both solutions before the *thioglycollic acid.*

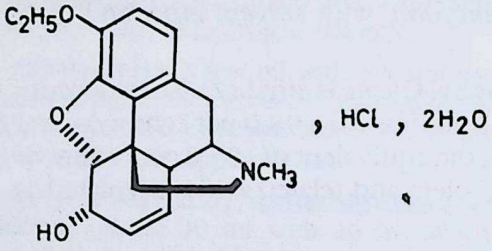
Heavy metals : Not more than 10 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

Cyanide : Dissolve 30.0 g in a mixture of 100 ml of *water* and 35 ml of *sodium hydroxide solution*, add 1 ml of a 0.02 per cent w/v solution of *dimethylaminobenzylidenerhodamine* in *acetone* and titrate with *0.01N silver nitrate* until the colour of the solution changes from yellow to orange. Repeat the operation without the disodium edetate; the difference between the titrations is not more than 1.25 ml.

Assay : Weigh accurately about 0.6 g and dissolve in sufficient *water* to produce 100 ml and titrate with the solution a mixture of 25.0 ml of *0.05M magnesium sulphate* and 10 ml of *strong ammonia-ammonium chloride solution*, using a mixture of 1 part by weight of *mordant black II*, 0.4 part by weight of *methyl orange*, and 100 parts by weight of *sodium chloride* as indicator. Each ml of *0.05M magnesium sulphate* is equivalent to 0.01861 g of $C_{10}H_{14}N_2Na_2O_8, 2H_2O$.

Storage : Store in well-closed containers.

Ethylmorphine Hydrochloride



$C_{19}H_{23}NO_3, HCl, 2H_2O$ Mol. Wt. 385.86

Category : Narcotic analgesic.

Dose : 6 to 30 mg.

Description : White, crystalline powder; odourless.

Solubility : Soluble in *water* and in *alcohol*; slightly soluble in *chloroform*; practically insoluble in *solvent ether.*

Standards : Ethylmorphine Hydrochloride is the dihydrate of the hydrochloride of O^3-ethylmorphine. It contains not less than 99.0 per cent of $C_{19}H_{23}NO_3, HCl$, calculated with reference to the dried substance.

Identification : (A) To 10 mg add 1 ml of *sulphuric acid* and 0.05 ml of a 1.3 per cent w/v solution of *ferric chloride* and heat on a water-bath; a blue colour is produced which changes to red on the addition of 0.05 ml of *nitric acid.*

(B) Dissolve 0.6 g in 6 ml of *water* in a test-tube and add 15 ml of *0.1N sodium hydroxide*; a white crystalline precipitate is formed on scratching the walls of the tube with a glass rod. Collect the precipitate, wash it with *water* and recrystallise from 5 ml of *water.* The crystals, after washing with *water* and drying "in vacuo", melt at about 85°, Appendix 5.11.

(C) A solution (1 in 100) gives the reactions of *chlorides*, Appendix 3.1.

Clarity and colour of solution : A 2.0 per cent w/v solution is clear and not more intensely coloured than a mixture of 1.2 ml of *ferric chloride C.S.*, 0.5 ml of *cobalt chloride C.S.*, 0.2 ml of *copper sulphate C.S.* and

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

sufficient *hydrochloric acid (1 per cent w/v HCl)* to produce 100 ml.

pH : Between 4.0 and 5.4, determined in a 2 per cent w/v solution, Appendix 5.10.

Specific optical rotation : Between −102° and −105°, determined at 20° in a solution prepared by dissolving 0.6 g in sufficient *water* to produce 30.0 ml, Appendix 5.12.

Morphine : Dissolve 0.1 g in sufficient *0.1N hydrochloric acid* to produce 5 ml, add 2 ml of a 1 per cent w/v solution of *sodium nitrite*, allow to stand for fifteen minutes and add 3 ml of *6N ammonia*. Any yellow or orange-yellow colour which appears is not more intense than that produced by treating 5 ml of a 0.0025 per cent w/v solution of *morphine hydrochloride* in *0.1N hydrochloric acid* in a similar manner.

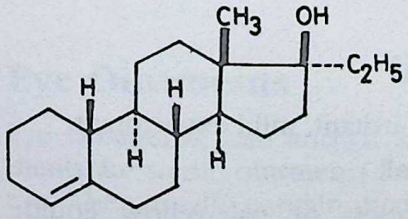
Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Between 8.0 per cent and 10.0 per cent, determined on 0.5 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.3 g, dissolve in 30 ml of *glacial acetic acid*, add 20 ml of *acetic anhydride* and 10 ml of *mercuric acetate solution* and titrate with *0.1N perchloric acid* using *crystal-violet solution* as indicator. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.03499 g of $C_{19}H_{23}NO_3$, HCl.

Storage : Store in well-closed, light-resistant containers.

Ethyloestrenol



$C_{20}H_{32}O$ Mol. Wt. 288.47

Category : Anabolic steroid.

Dose : 2 to 4 mg daily.

Description : White or almost white, crystalline powder; odourless.

Solubility : Practically insoluble in *water*; soluble in *alcohol*; freely soluble in *chloroform* and in *solvent ether*.

Standards : Ethyloestrenol is 17*α*-ethylestr-4-en-17*β*-ol, containing a varying amount of methyl alcohol of crystallisation. It contains not less than 95.0 per cent and not more than the equivalent of 103.0 per cent of $C_{20}H_{32}O$, calculated with reference to the dried and methyl alcohol-free substance.

Identification : (A) The light absorption in the range 230 to 350 nm, of a 0.5 per cent w/v solution in *methyl alcohol* exhibits no maximum, Appendix 5.15 A.

(B) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 4 volumes of *heptane* and 1 volume of *acetone* as the mobile phase, allowing the solvent to ascend 10 cm above the line of application. Apply separately to the plate 2 µl of each of two solutions in a mixture of 9 volumes of *chloroform* and 1 volume of *methyl alcohol* containing (1) 0.25 per cent w/v of the substance being examined and (2) 0.25 per cent w/v of *ethyloestrenol R.S.* and at a third point apply 2 ul of a mixture, of equal volume of solutions (1) and (2). After removal of the plate, heat it at 105° for ten minutes, spray with a 10 per cent v/v solution of *sulphuric acid* in *alcohol*, heat at 105° for a further ten minutes, allow to cool, and examine in daylight and under an ultra-violet lamp having a maximum output at about 366 nm. The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2). The principal spot in the third chromatogram appears as a single compact spot.

(C) It melts at about 89°, Appendix 5 11.

Specific optical rotation : Between +29° and +33°, determined in a 1.0 per cent w/v solution in *dioxan*, Appendix 5.12.

Methyl alcohol : Not more than 4.0 per cent w/w. Carry out the method for *gas-liquid chromatography*, Appendix 5.4.1, using solutions in *acetone* containing (1) 0.4 per cent v/v of *methyl alcohol*, and 0.4 per cent v/v of *ethyl alcohol* (internal standard), (2) 10 per cent w/v of the substance being examined, and (3) 10 per cent w/v of the substance being examined and 0.4 per cent v/v of the internal standard. The chromatographic procedure may be carried out using (a) a column 2 m long and 0.4 mm in internal diameter packed with porous polymer beads (100 to 120 mesh) (Porapak Q is suitable) and maintained at 170°, (b) *nitrogen* as the carrier gas, and (c) a flame ionisation detector. Calculate the percentage w/w of methyl alcohol, assuming the weight per ml, at 20° , to be 0.792 g.

17*α*-Ethylestran-17*β*-ol : Examine by *gas-liquid chromatography*, Appendix 5.4.1, using two solutions in *chloroform* containing (1) 0.004 per cent w/v of *17α-ethylestran-17β-ol R.S.* and (2) 0.2 per cent w/v of the substance being examined. The chromatographic conditions described under the Assay may be used. In the chromatogram obtained with solution (2) the area of the peak due to 17*α*-ethylestran-17*β*-ol is not greater than 2 per cent of the area of the peak due to ethyloestrenol.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying "in vacuo" for 24 hours, Appendix 5.8.

Assay : Carry out the method for *gas-liquid chromatography*, Appendix 5.4.1, using three solutions in *chloroform* containing (1) 0.1 per cent w/v of *arachidic alcohol* (internal standard) and 0.2 per cent w/v of *ethyloestrenol R.S.*, (2) 0.2 per cent w/v of the substance being examined, and (3) 0.2 per cent w/v of the substance being examined and 0.1 per cent w/v of the internal standard. The chromatographic procedure may be carried out using : (a) a glass column 1.0 m long and 0.4 cm in internal diameter packed with 3 per cent w/w of phenylmethyl silicone fluid (50 per cent phenyl) (OV 17 is suitable) on acid-washed, silanised diatomaceous earth (80 to 100 mesh) and maintained at 200°; (b) *nitrogen* as the carrier gas; and (c) a flame ionisation detector. Calculate the content of $C_{20}H_{32}O$ using the declared content of $C_{20}H_{32}O$ in *ethyloestrenol R.S.*

Storage : Store in well-closed light-resistant containers at a temperature not exceeding 15°.

Ethyloestrenol Tablets

Category : Anabolic steroid.

Dose : Ethyloestrenol, 2 to 4 mg daily.

Usual strength : 2 mg.

Standards : Ethyloestrenol Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Ethyloestrenol, $C_{20}H_{32}O$.

Identification : (A) Comply with **Identification** test (B) described under Ethyloestrenol, using the following solutions: For solution (1) extract a quantity of the powdered tablets equivalent to 1 mg of Ethyloestrenol with *chloroform*, filter, evaporate the filtrate to dryness at room temperature under reduced pressure and dissolve the residue in 0.4 ml of a mixture of 9 volumes of *chloroform* and 1 volume of *methyl alcohol*. Solution (2) is a 0.25 per cent w/v solution of *ethyloestrenol R.S.* in a mixture of 9 volumes of *chloroform* and 1 volume of *methyl alcohol*.

(B) In the **Assay**, the chromatogram obtained with solution (2) shows a peak having the same retention time as the peak due to *ethyloestrenol R.S.* in the chromatogram obtained with solution (1).

17α-Ethyloestran-17β-ol : Comply with the test described under Ethyloestrenol, using the following as solution (2): Extract a quantity of the powdered tablets equivalent to 2 mg of Ethyloestrenol with 20 ml of *acetone*, filter evaporate the filtrate to dryness on a water-bath, and dissolve the residue in 1 ml of *chloroform*.

Uniformity of content : Proceed as directed in the **Assay**, using as solution (2) the following: Powder one tablet and extract with 5 ml of *chloroform* in a centrifuge tube. Centrifuge; evaporate 2.0 ml of the supernatant liquid in a current of *nitrogen* and dissolve the residue in 2.0 ml of *acetone*. Evaporate the solution to dryness on a water-bath and dissolve the residue in 0.4 ml of *chloroform*. Solution (3) is prepared in a similar manner on 2.0 ml of the supernatant liquid but by extracting with 2.0 ml of a 0.02 per cent w/v solution of *arachidic alcohol* in *acetone*. Calculate the content of $C_{20}H_{32}O$ in the tablet.

Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 90 and 110 per cent of the average except that for one tablet the content may be between 85 and 115 per cent of the average.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Carry out the method for *gas-liquid chromatography*, Appendix 5.4.1, using the following solutions : Solution (1) is a solution in *chloroform* containing 0.1 per cent w/v of *arachidic alcohol* (internal standard) and 0.2 per cent w/v of *ethyloestrenol R.S.* For solution (2) extract a quantity of the powdered tablets equivalent to 8 mg of Ethyloestrenol with 20 ml of *acetone*, filter, evaporate the filtrate to dryness on a water-bath, and dissolve the residue in 4 ml of *chloroform*. Solution (3) is prepared in a similar manner but extracting with 20 ml of a 0.02 per cent w/v solution of *arachidic alcohol* in *acetone*. Calculate the content of $C_{20}H_{32}O$ from the declared content of $C_{20}H_{32}O$ in *ethyloestrenol R.S.*

Storage : Preserve in well-closed, light-resistant containers in cool place.

Eucalyptus Oil

Category : Counter-irritant, mild expectorant.

Dose : 0.06 to 0.2 ml.

Description : Colourless or pale-yellow liquid; odour, aromatic, and camphoraceous; taste, pungent and camphoraceous, followed by a sensation of cold

Solubility : Sparingly soluble in *alcohol (80 per cent)*.

Standards : Eucalyptus oil is the essential oil obtained by steam distillation and rectification from the fresh leaves of *Eucalyptus globulus* Labill or from other species of *Eucalyptus* (Fam. Myrtaceae). It contains not less than 65.0 per cent w/w of Cineole, $C_{10}H_{18}O$.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Optical rotation : Between 0° and +10°, Appendix 5.12.

Wt. per ml : Between 0.897 and 0.916 g, Appendix 5.19.

Refractive index : Between 1.457 and 1.469, Appendix 5.14.

Phellandrene : Mix 1 ml with 2 ml of *glacial acetic acid* and 5 ml of *light petroleum (boiling range 60° to 80°)*, add 2 ml of a saturated solution of *sodium nitrite* and shake the mixture gently; no crystalline precipitate is formed in the upper layer.

Aldehydes : Place 10 ml in a glass-stoppered tube about 25 mm in diameter and 150 mm long, add 5 ml of *benzene* and 4 ml of *hydroxylamine hydrochloride reagent in alcohol (60 per cent)*. Shake vigorously and titrate immediately with *0.5N potassium hydroxide in alcohol (60 per cent)* until red colour changes to yellow. Continue shaking and neutralising until the full yellow colour of the indicator is permanent in the lower layer after shaking vigorously for 2 minutes and allowing separation to take place. The reaction is complete in about 15 minutes. Repeat the operation using a further 10 ml of the eucalyptus oil and, as the reference solution for the end-point, the titrated liquid of the first determination with the addition of 0.5 ml of *0.5N potassium hydroxide* in *alcohol (60 per cent)*. Not more than 2.0 ml of *0.5N potassium hydroxide* is required in the second determination.

Heavy metals : Not more than 40 parts per million, determined by Method B on 0.5 g, Appendix 3.2.4.

Assay : Carry out the method for the *determination of cineole*, Appendix 3.3.29.

Storage : Store in well-closed light-resistant containers in a cool place.

Eye Ointments

Eye Ointments, also known as Ophthalmic Ointments are sterile ointments for application to the eye. They usually contain medicaments with antiseptic, anti-inflammatory, antimicrobial, mydriatic or miotic properties. They may contain suitable antioxidants, stabilising agents and antibacterial preservatives.

Special precautions should be taken in the preparation of eye ointments. They are manufactured from sterilised ingredients under rigidly aseptic conditions. Where the specific ingredients used do not lend themselves to routine sterilisation methods, ingredients that comply with the *tests for sterility*, along with aseptic manufacture, may be employed.

Preparation of eye ointments : The ointment base selected must be non-irritating to the eye, allow the drug to diffuse throughout the secretions of the eye and retain the activity of the medicament for a reasonable period of time under stated storage conditions.

A commonly used base consists of varying proportions of Soft Paraffin, Hard Paraffin and Liquid Paraffin with or without wool fat. For water-soluble drugs absorption bases or water-soluble or water-removable bases may be used. The ointment is generally prepared, by means of an aseptic technique, by either of the following methods using apparatus which has been thoroughly cleaned and Sterilised:

(a) If the medicament dissolves in water to give a stable solution, it is dissolved in the minimum quantity of *water*, the solution is Sterilised and then incorporated gradually in a melted sterile base, the mixture being stirred continuously until it is cold. The ointment is then transferred to the final sterile containers which are then closed so as to exclude micro-organisms.

(b) If it is not soluble in water, the sterile medicament is reduced to an extremely fine powder, thoroughly mixed with a small quantity of the melted sterile base and then incorporated with the remainder of the sterile base. The ointment is then transferred to the final containers which are then closed so as to exclude micro-organisms.

Requirements of Tests

The finished ointment must be homogeneous, and free from lumps and large particles and must comply with the following requirements:

1. Sterility : Complies with the *test for sterility*, Appendix 4.6, using the *membrane filtration method* for ointments soluble in *isopropyl myristate*, and the *direct inoculation method* for ointments insoluble in *isopropyl myristate*.

2. Particle size : Gently spread a small quantity of the ointment as a thin layer on a microscope slide. Scan under a microscope an area corresponding to 10 µg of the solid phase. Not more than ten particles have a maximum dimension greater than 50 µm and none has a maximum dimension greater than 100 µm.

General Requirements

1. Packing : Eye Ointments should be packed in sterilised, collapsible tubes of metal or of suitable plastic fitted or provided with a nozzle of suitable shape to facilitate the application of the product without contamination and with a cap; the usable contents of such packs should not exceed 5 g. Eye ointments may also be packed in quantities sufficient for application on one occasion, in appropriately treated gelatin or other suitable containers of such a shape as to facilitate administration without contamination; such containers should be individually wrapped.

Collapsible tubes should be as free as possible from contaminants. The cap is covered with an easily-removable seal, or the package or carton may be suitably

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

sealed to prevent removal of the contents without the seal being broken.

Metal collapsible tubes should comply with the following test for metal particles.

Select a sample of fifty tubes from the batch to be tested, and clean each tube by vibration and/or "blowing". Fill the tubes with suitable molten eye ointment, close the open end of the tube by a double fold and allow the filled tubes to cool overnight at a temperature of 15° to 20°.

Assemble a metal bacteriological filter with a 4.25 cm filter paper of suitable porosity supported on a suitable perforated plate in place of the standard sintered carbon disc and heat it in a suitable manner to a temperature above the melting range of the base.

Remove the caps from the cooled tubes and apply uniform pressure to the closed end of each tube in turn, in such a manner that the time taken to express, as much of the base, as possible through each nozzle is not less than 20 seconds in each case. Collect the extruded bases from the fifty tubes in the heated filter, applying suction to the stem of the filter in order to draw the molten base through the filter paper. When all the melted base has been removed, wash the walls of the filter and the filter paper with three successive 30-ml portions of *chloroform*, allow the filter paper to dry, and immediately mount it between glass for examination.

Examine the filter paper under oblique lighting with the aid of a magnifying glass with a graticule of 1 mm squares, one of which is sub-divided into 0.2 mm squares and note:

(a) The number of all metal particles 1 mm in length and longer.

(b) The number in the range 0.5 mm to less than 1 mm.

(c) The number in the range 0.2 mm to less than 0.5 mm.

Carry out two further examinations with the filter paper in two different positions so that the lighting comes from different directions, and calculate the average number of metal particles counted in each of the three ranges specified. Given each metal particle detected on the filter papers a score as follows and add the scores together:

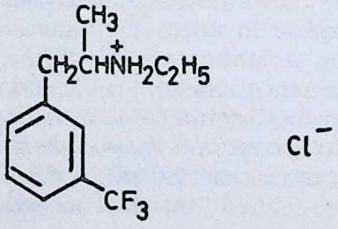
Particles 1 mm and above	50
Particles 0.5 mm but less than 1 mm	10
Particles 0.2 mm but less than 0.5 mm	2
Particles less than 0.2 mm	Nil

The batch of tubes passes the test if the total score is less than 100 points; if the total score is more than 150 points the batch fails the test. If the total score between 100 and 150 points inclusive the test is repeated on a further sample of 50 tubes and the batch passes the test if the sum of the total scores in the two tests is less than 150 points.

A batch for sampling will normally be either the manufacturer's day's production or a consignment delivered to the tube user.

Labelling : Comply with the requirements for Labelling specified in the individual monograph, if any. The label on the tube or outer envelope also states:(1) that the contents are sterile provided that the container has not been opened; (2) the names and proportions of any added anti-oxidant, stabilising agent or antimicrobial preservative; (3) storage conditions.

Fenfluramine Hydrochloride



$C_{12}H_{16}F_3N, HCl$ Mol. Wt. 267.74

Category : Appetite suppressant.

Dose : 40 to 80 mg daily in divided doses.

Description : White crystalline powder; odourless; taste, slightly bitter.

Solubility : Soluble in *water*, in *alcohol* and in *chloroform*; practically insoluble in *solvent ether*.

Standards : Fenfluramine Hydrochloride is *N*-ethyl-α-methyl-3-trifluoromethyl-phenethylammonium chloride. It contains not less than 98.5 per cent and not more than the equivalent of 101.0 per cent of $C_{12}H_{16}F_3N, HCl$, calculated with reference to the dried substance.

Identification : (A) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 100 volumes of *methyl alcohol* and 1.5 volumes of strong *ammonia solution* as the mobile phase. Apply separately to the plate 10 µl of each of two solutions in *chloroform* containing (1) per cent w/v of the substance being examined and (2) 1 per cent w/v of *fenfluramine hydrochloride R.S.* After removal of the plate, allow it to dry in air and spray with *dilute potassium iodobismuthate solution*. The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

(B) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

Melting range : Between 168° and 172°, Appendix 5.11.

Foreign substances : Carry out the method for *gas-liquid chromatography*, Appendix 5.4.1, using the following solutions: (1) dissolve 8 mg of *fenfluramine hydrochloride R.S.* in 100 ml of *water* and add 10 ml of a 20 per cent w/v solution of *potassium hydroxide*; extract with four quantities, each of 25 ml, of *chloroform*, filter and evaporate the combined filtrates to dryness, removing the final solvent in a current of *nitrogen*; dissolve the residue in 10 ml of a 0.01 per cent v/v solution of *NN-diethylaniline* (internal standard) in *chloroform*; (2) treat 0.40 g of the substance being examined in a similar manner; (3) treat 0.40 g of the substance being examined in a similar manner but dissolve the residue from the chloroform extraction in 10 ml of *chloroform*. The chromatographic procedure may be carried out using (a) a glass column 2.75 m long and 0.4 cm in internal diameter packed with 10 per cent w/w of Carbowax 20 M and 2 per cent w/w of *potassium hydroxide* supported on acid washed diatomaceous earth (80 to 100 mesh) maintained at 135°, (b) nitrogen as the carrier gas, and (c) a flame ionisation detector maintained at 200°. In the chromatogram obtained with solution (2) the ratio of the area of the peak corresponding to the internal standard to that of the peak occurring immediately after the main peak is not less than the ratio of the area of the peak corresponding to the internal standard to that of the peak corresponding to fenfluramine in the chromatogram obtained with solution (1).

Heavy metals : Not more than 20 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.3 g, dissolve in a mixture of 50 ml *chloroform* and 20 ml *acetone*, add 10 ml of *mercuric acetate solution* and titrate with *0.1N perchloric acid* determining the end-point potentiometrically. Perform a blank titration and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02677 g of $C_{12}H_{16}F_3N$, HCl.

Storage : Store in tightly-closed, light-resistant containers.

Fenfluramine Tablets

Category : Appetite suppressant.

Dose : Fenfluramine Hydrochloride, 40 to 120 mg daily, in divided doses.

Usual strength : 20 mg.

Standards : Fenfluramine Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Fenfluramine Hydrochloride, $C_{12}H_{16}F_3N$, HCl. The tablets may be coated.

Identification : Comply with **Identification** test (A) described under Fenfluramine Hydrochloride, using as solution (1) a solution prepared by shaking a quantity of the powdered tablets equivalent to 0.1 g of Fenfluramine Hydrochloride with 10 ml of *chloroform* and filtering.

Other requirements : Comply with the requirements stated under Tablets.

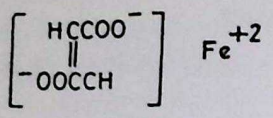
Assay : Carry out the method for *gas-liquid chromatography*, Appendix 5.4.1, using the following solutions: (1) dissolve 0.1 g of *fenfluramine hydrochloride R.S.* in 100 ml of *water*, add 10 ml of a 20 per cent w/v solution of *potassium hydroxide*, extract with four quantities, each of 25 ml of *chloroform*, filter, and evaporate the combined filtrates to dryness, removing the final solvent in a current of *nitrogen*; dissolve the residue in 10 ml of a 0.4 per cent v/v solution of *n-tetradecane* (internal standard) in *chloroform*; (2) weigh and powder 20 tablets; weigh accurately a quantity of the powder equivalent to 0.20 g of Fenfluramine Hydrochloride and shake with 80 ml of *water* for one hour, filter, and add sufficient *water* to produce 100 ml. To 50 ml of the filtrate add 50 ml of *water* and complete the procedure described under solution (1) beginning at the words "add 10 ml ..." but dissolving the residue from the chloroform extraction in 10 ml of *chloroform* containing 0.4 per cent v/v of *n-tetradecane* and 0.0025 per cent v/v of *NN-diethylaniline*; (3) to the remainder of the filtrate obtained under (2) add 50 ml of *water* and complete the procedure under solution (1) beginning at the words "add 10 ml ..." but dissolving the residue from the chloroform extraction in 10 ml of *chloroform*. Carry out the chromatographic procedure using : (a) a glass column 2.75 m long and 4 mm in internal diameter packed with 10 per cent w/w of Carbowax 20 M and 2 per cent w/w of *potassium hydroxide* supported on acid-washed diatomaceous earth (80 to 100 mesh) maintained at 135°, (b) *nitrogen* as the carrier gas, and (c) a flame ionisation detector maintained at 200°. Calculate the content of $C_{12}H_{16}F_3N$, HCl using the declared content of $C_{12}H_{16}F_3N$, HCl in *fenfluramine hydrochloride R.S.*

Storage : Store in tightly-closed, light-resistant containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Ferrous Fumarate



$C_4H_2FeO_4$ Mol. Wt. 169.91

Category : Haematinic.

Dose : 0.2 to 0.6 g daily.

Description : Reddish-orange to reddish-brown fine powder; may contain soft lumps that produce a yellow streak when crushed; odour, slight; taste, slightly astringent.

Solubility : Slightly soluble in *water*; very slightly soluble in *alcohol.*

Standards : Ferrous Fumarate contains not less than 93.0 per cent of $C_4H_2FeO_4$, calculated with reference to the dried substance.

Identification : (A) Heat 1 g with 25 ml of a mixture of equal volumes of *hydrochloric acid* and *water* on a water-bath for fifteen minutes; cool and filter. The filtrate gives the reactions of *ferrous salts*, Appendix 3.1. Wash the precipitate with a mixture of one volume of *dilute hydrochloric acid* and nine volumes of *water* and dry at 100°. Suspend 0.1 g of the residue in 2 ml of *sodium carbonate solution* and add *potassium permanganate solution*, dropwise; the permanganate is decolorised and a brownish solution is obtained.

(B) Mix 0.5 g with 1 g of *resorcinol.* To 0.5 g of the mixture in a crucible, add a few drops of *sulphuric acid* and heat gently; a deep-red, semi-solid mass is formed. Add the mass to a large volume of *water*; an orange-yellow solution without any fluorescence is obtained.

Arsenic : Not more than 5 parts per million, Appendix 3.2.1.

Heavy metals : Not more than 20 parts per million, determined by the following methods: Ignite 1.0 g gently until free from carbon, dissolve in 5 ml of *hydrochloric acid Sp.* by heating on a water-bath, and evaporate to dryness. Dissolve the residue in a mixture of 15 ml of *hydrochloric acid Sp.*, 4 ml of *nitric acid Sp.* and 6 ml of *water*; boil gently for one minute, cool and extract with three quantities, each of 20 ml, of *solvent ether.* If the acid layer is more than slightly yellow, extract with a further quantity of 20 ml of *solvent ether*; reject the extracts, heat the acid solution gently to remove the ether, add 1 g of *citric acid*, make alkaline with *5N ammonia* and add 1 ml of *potassium cyanide solution Sp.* Dilute to 50 ml with *water.* Add 0.1 ml of *sodium sulphide solution.* Any brown colour produced is not more intense than that produced by treating 2.0 ml of *standard lead solution* in a similar manner.

Sulphate : Boil 0.3 g with 10 ml of *dilute hydrochloric acid* and 30 ml of *water*, cool with ice, and filter; the filtrate complies with the *limit test for sulphates*, Appendix 3.2.8.

Ferric iron : Not more than 2.0 per cent, determined by the following method: Weigh accurately about 3 g and dissolve in a mixture of 200 ml of *water* and 20 ml of *hydrochloric acid* by heating rapidly to boiling point. Boil for fifteen seconds, cool rapidly, add 3 g of *potassium iodide*, allow to stand in the dark for fifteen minutes, and titrate the liberated iodine with *0.1N sodium thiosulphate*, using *starch solution* as indicator.

Repeat the operation without the ferrous fumarate; the difference between the titrations represents the amount of iodine liberated by the ferric iron. Each ml of *0.1N sodium thiosulphate* is equivalent to 0.005585 g of ferric iron.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.3 g and dissolve in 15 ml of *dilute sulphuric acid* with the aid of gently heat. Cool, add 50 ml of *water*, and immediately titrate with *0.1N ceric ammonium sulphate*, using *ferroin sulphate solution* as indicator. Each ml of *0.1 N ceric ammonium sulphate* is equivalent to 0.01699 g of $C_4H_2FeO_4$.

Storage : Store in well-closed containers.

Ferrous Fumarate Tablets

Category : Haematinic.

Dose : Ferrous Fumarate. Prophylactic, 0.2 g daily; therapeutic, 0.4 to 0.6 g daily, in divided doses.

Usual strength : 0.2 g.

Standards : Ferrous Fumarate Tablets contain not less than 90.0 per cent and not more than 105.0 per cent of the stated amount of Ferrous Fumarate $C_4H_2FeO_4$.

Identification : The powdered tablets comply with **Identification** tests (A) and (B) described under Ferrous Fumarate.

Ferric iron : Carry out the test described under Ferrous Fumarate, using a quantity of powder prepared for the **Assay** equivalent to 3.0 g of Ferrous Fumarate. The difference between the titrations is not more than 13.5 ml.

Disintegration : Maximum time, 1 hour, Appendix 5.6.1.

Other requirements : Comply with the requirements stated under Tablets.

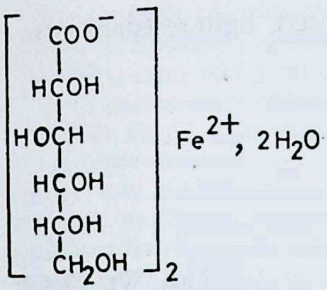
CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.3 g of Ferrous Fumarate and carry out the **Assay** described under Ferrous Fumarate. Each ml of *0.1 N ceric ammonium sulphate* is equivalent to 0.01699 g of $C_4H_2FeO_4$.

Storage : Store in light-resistant containers.

Ferrous Gluconate



$C_{12}H_{22}FeO_{14}, 2H_2O$ Mol. Wt. 482.17

Category : Haematinic.

Dose : Prophylactic, 600 mg daily. Therapeutic, 1.2 to 1.8 g daily in divided doses.

Description : Yellowish-grey or pale greenish-yellow, fine powder or granules; odour, slight, resembling that of burnt sugar.

Solubility : Fairly soluble in *water*; more readily soluble on warming, almost insoluble in *alcohol*.

Standards : Ferrous Gluconate contains not less than 95.0 per cent of $C_{12}H_{22}FeO_{14}$, calculated with reference to the dried substance.

Identification : (A) A solution (1 in 20) gives the reactions of *ferrous salts*, Appendix 3.1.

(B) To 0.75 g in a test-tube add 7.5 ml of warm *water*, add 1 ml of *glacial acetic acid*, and 1 ml of freshly distilled *phenylhydrazine*. Heat the mixture on a water-bath for thirty minutes. Cool, and scratch the inner surface of the tube with a glass rod until crystals of gluconic acid phenylhydrazide begin to form. Set aside for ten minutes, filter, dissolve the precipitate in hot *water*, mix a small amount of *decolorising charcoal* and filter in a tube. Allow the filtrate to cool, and scratch the inner surface of the tube; white crystals are obtained which melt at about 202°, with decomposition, Appendix 5.11.

Clarity and colour of solution : A 10 per cent w/v solution in *carbon dioxide-free water* is clear and greenish-brown in colour.

Acidity : A 5.0 per cent w/v solution is acid to *litmus solution*.

Arsenic : Not more than 2 parts per million, Appendix 3.2.1.

Barium : Dissolve 0.1 g in 50 ml of *water*, and 5 ml of *dilute sulphuric acid*, and allow to stand for five minutes; no turbidity is produced.

Ferric iron : Not more than 1.0 per cent, determined by the following method: Weigh accurately about 5 g and transfer to a glass-stoppered flask and dissolve in 100 ml of freshly boiled and cooled *water* and 10 ml of *hydrochloric acid* and add 3 g of *potassium iodide*. Shake well and allow to stand in the dark for five minutes. Titrate any liberated iodide with *0.1N sodium thiosulphate*, using *starch solution* as indicator. Perform a blank determination and make any necessary correction. Each ml of *0.1N sodium thiosulphate* is equivalent to 0.005585 g of ferric iron.

Heavy metals : Not more than 20 parts per million, determined by Method A, Appendix 3.2.4, on a solution prepared in the following manner: Warm 2 g gently with 10 ml of *nitric acid Sp.* until reaction begins and allow to stand until the evolution of nitrous fumes subsides. Boil gently to complete oxidation, adding a further 5 ml of *nitric acid Sp.*, if necessary, and continue boiling until the volume is reduced to about 5 ml. Add 20 ml of *hydrochloric acid Sp.*, boil gently for one minute, cool, and transfer to a separator. Extract with three quantities, each of 20 ml, of *solvent ether*, and, if the acid solution is still more than faintly yellow, with a fourth quantity of 20 ml of *solvent ether*, reject the ether extracts. Transfer the acid solution to a narrow necked flask, rinse the separator with 5 ml of *water*, and add the rinsings to the flask. Heat to remove dissolved ether and part of the hydrochloric acid. Cool and dilute to 50 ml with *water*. Use 25 ml for the test.

Chloride : 0.5 g complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphate : 1 g complies with the *limit test for sulphates*, Appendix 3.2.8.

Oxalic acid : Dissolve 1 g in 5 ml of *water*, add 2 ml of *hydrochloric acid* and transfer to a separator. Extract with two quantities, each of 20 ml, of *solvent ether*. Evaporate the combined ether extracts to dryness on a water-bath and dissolve the residue in 5 ml of *water*. Add 1 drop of *acetic acid* and 3 ml of *calcium chloride solution*, no turbidity is produced.

Reducing sugars : Dissolve 0.5 g in 10 ml of *water* and make alkaline with *dilute ammonia solution*. Pass *hydrogen sulphide* into the solution and allow to stand for thirty minutes. Filter, and wash the precipitate with two quantities, each of 5 ml, of *water*. Combine the filtrate and the washings, and acidify with *hydrochloric acid*. Add 2 ml of *dilute hydrochloric acid* in excess. Boil the solution until the vapours no longer darken *lead acetate paper* and, if necessary, boil further to concentrate the solution to 10 ml. Cool and add 10 ml of *sodium carbonate solution*, set aside for five minutes, filter, and

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

dilute the filtrate with *water* to 100 ml. To 5 ml of the filtrate add 2 ml of *potassium cupri-tartrate solution* and boil for one minute; no red precipitate is formed within one minute.

Loss on drying : Not less than 5.0 per cent and not more than 10.0 per cent, determined on 1.0 g by drying in an oven at 105° for four hours, Appendix 5.8.

Assay : Weigh accurately about 1.5 g and dissolve in a mixture of 75 ml of *water* and 15 ml of *2N sulphuric acid*. Add 0.75 g of *zinc powder*, stopper the flask and allow to stand for about twenty minutes until the solution is decolorised. Drain the precipitate onto a glass filter or which has been deposited a thin layer of *zinc powder*, and wash the filter with 20 ml of *carbon dioxide-free water*. To the combined filtrate and washings add 0.2 ml of *ferrous sulphate solution* and titrate with *0.1N ceric ammonium sulphate* until the colour changes from orange to green. Perform a blank determination and make any necessary correction. Each ml of *0.1N ceric ammonium sulphate* is equivalent to 0.04461 g of $C_{12}H_{22}FeO_{14}$.

Storage : Store in well-closed, light-resistant containers.

Ferrous Gluconate Tablets

Category : Haematinic.

Dose : Ferrous Gluconate, 0.3 to 0.6 g.

Usual strength : 0.3 g.

Standards : Ferrous Gluconate Tablets contain not less than 90.0 per cent and not more than 105.0 per cent of the stated amount of Ferrous Gluconate, $C_{12}H_{22}FeO_{14}, 2H_2O$. The tablets may be coated.

Identification : (A) Dissolve a quantity of the powdered tablets, equivalent to about 1 g of Ferrous Gluconate in 10 ml of *water*, and filter; the solution complies with **Identification** tests (A) and (B) described under Ferrous Gluconate.

(B) Shake a quantity of the powdered tablets, equivalent to 0.5 g of Ferrous Gluconate with 10 ml of *dilute hydrochloric acid*, filter, and add to the filtrate, 1 ml of *barium chloride solution*; an opalescence may be produced but no precipitate is formed.

Ferric iron : Dissolve a quantity of the powder prepared for the **Assay**, equivalent to 2.0 g of Ferrous Gluconate in a stoppered flask as completely as possible without the aid of heat in a mixture of 100 ml of freshly boiled and cooled *water* and 10 ml of *hydrochloric acid*, and add 3.0 g of *potassium iodide*, close the flask, allow to stand in the dark for five minutes, and titrate the liberated iodine with *0.1N sodium thiosulphate*, using *starch solution* as indicator. Repeat the operation without the powder. The difference between the titrations is not more than 7.5 ml.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 1.5 g of Ferrous Gluconate, and complete the **Assay** described under Ferrous Gluconate beginning at the words "dissolve in a mixture....". Each ml of *0.1N ceric ammonium sulphate* is equivalent to 0.04822 g of $C_{12}H_{22}FeO_{14}, 2H_2O$.

Storage : Store in well-closed, light-resistant containers.

Ferrous Sulphate

$FeSO_4, 7H_2O$ Mol. Wt. 278.0

Category : Haematinic.

Dose : 0.2 to 0.3 g.

Description : Transparent, green crystals, or a pale bluish-green, crystalline powder; odourless; taste, metallic and astringent. Efflorescent in dry air. On exposure to moist air, the crystals rapidly oxidise and become coated with brownish-yellow basic ferrous sulphate.

Solubility : Freely soluble in *water*, very soluble in boiling *water*, practically insoluble in *alcohol*.

Standards : Ferrous Sulphate contains not less than 98.0 per cent and not more than the equivalent of 105.0 per cent of $FeSO_4, 7H_2O$.

Identification : A solution (1 in 20) gives the reactions of *ferrous salts*, and of *sulphates*, Appendix 3.1.

pH : Between 3.0 and 4.0, determined in a 5.0 per cent w/v solution, Appendix 5.10.

Arsenic : Not more than 2 parts per million, Appendix 3.2.1.

Copper, Zinc and Lead : Dissolve 8.0 g in 40 ml of *hydrochloric acid*, add 10 ml of *nitric acid* and 15 ml of *water*, boil gently for five minutes and cool. Shake with four quantities, each of 30 ml, of *solvent ether* and discard the ether. Heat the acid solution on a water-bath to remove dissolved ether, cool and add sufficient *water* to produce 100.0 ml (solution A).

Copper : To 10.0 ml of solution A obtained in the test for **Copper, Zinc and Lead**, add 1 g of *citric acid*, make alkaline with *dilute ammonia solution* and add 25 ml of *water* and 5 ml of *sodium diethyldithiocarbamate*

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

solution. Extract with 5,3 and 2 ml of *carbon tetrachloride*. Add sufficient *carbon tetrachloride* to produce 10.0 ml. The colour of the resulting solution is not greater than that of a solution prepared by treating 2.5 ml of *dilute copper sulphate solution* and 7.5 ml of *water* in the same manner.

Zinc : To 10 ml of solution A add 1 g of *citric acid* and 1 g of *resorcinol*, neutralise with *dilute ammonia solution*, using *thymol blue solution* as indicator, and shake for one minute with two successive quantities, each of 20 ml, of *dithizone solution*. To the combined extracts, add 10 ml of *0.1N hydrochloric acid* and shake for one minute separate the acid layer, and wash with 2 ml of *chloroform*. To the acid layer add 3 ml of *N hydrochloric acid* and 20 ml of *ammonium chloride solution* and adjust the volume to 50 ml with *water*. Add 1 ml of *potassium ferrocyanide solution* and allow to stand for fifteen minutes. Any turbidity produced is not greater than that developed in fifteen minutes by the addition of 1 ml of *potassium ferrocyanide solution*; to a freshly prepared mixture of 4 ml of *dilute zinc sulphate solution*, 4 ml of *N hydrochloric acid*, 20 ml of *ammonium chloride solution* and sufficient *water* to produce 50.0 ml.

Lead : Make 40 ml of solution A alkaline with *dilute ammonia solution Sp.*, add 1 ml of *potassium cyanide solution Sp.* and sufficient *water* to produce 50 ml. Add 0.1 ml of *sodium sulphide solution*. The solution is not more intensely coloured than a mixture of 10 ml of *hydrochloric acid Sp.*, 0.5 ml of *nitric acid Sp.*, 10 ml of *standard lead solution*, 0.1 ml of *sodium sulphide solution* and sufficient *water* to produce 50 ml.

Manganese : Dissolve 1.0 g in 40 ml of *water*, add 10 ml of *nitric acid* and boil until red fumes cease to be evolved. Add 0.5 g of *ammonium persulphate* and boil for ten minutes. If any pink colour develops, decolorise the solution by dropwise addition of a 5 per cent w/v solution of *sodium sulphite* and boil until the odour of *sulphur dioxide* is not discernible. Add 10 ml of *water*, 5 ml of *phosphoric acid* and 0.5 g of *sodium periodate*, boil for one minute and cool. The colour of the solution is not deeper than that of a solution containing the same quantities of the same reagents and 1.0 ml of *0.1N potassium permanganates*.

Oxysulphate : 1 g dissolved in 2 ml of freshly boiled and cooled *water* forms a clear solution which is not more than faintly turbid.

Assay : Weigh accurately about 1 g, dissolve in a mixture of 30 ml of *water* and 20 ml of *dilute sulphuric acid* and titrate with *0.1N ceric ammonium sulphate* using *ferroin sulphate solution* as indicator. Each ml of *0.1 N ceric ammonium sulphate* is equivalent to 0.0278 g of $FeSO_4, 7H_2O$.

Storage : Store in tightly-closed containers.

Dried Ferrous Sulphate

Category : Haematinic.

Dose : Prophylactic, 200 mg daily; therapeutic, 400 to 600 mg daily, in divided doses.

Description : Greyish-white to buff-coloured powder; taste, metallic and astringent.

Solubility : Slowly soluble in freshly boiled and cooled *water*; practically insoluble in *alcohol*.

Standards : Dried Ferrous Sulphate is Ferrous Sulphate deprived of part of its water of crystallisation by drying at 40°. It contains not less than 80.0 per cent and not more than 90.0 per cent of $FeSO_4$.

Identification : A solution (1 in 20) gives the reactions of *ferrous salts*, and of *sulphates*, Appendix 3.1.

Arsenic : Not more than 3 parts per million, Appendix 3.2.1.

Copper, Zinc and Lead : Complies with the test described under Ferrous Sulphate, using 4.5 g of the substance being examined.

Manganese : Complies with the test described under Ferous Sulphate, using 0.5 g of the substance being examined.

Oxysulphate : 2 g dissolved slowly in a mixture of 7.5 ml of freshly boiled and cooled *water* and 0.5 ml of *N sulphuric acid* forms a solution which is not more than faintly turbid.

Assay : Weigh accurately about 0.5 g, and carry out the **Assay** described under Ferrous Sulphate. Each ml of *0.1N ceric ammonium sulphate* is equivalent to 0.01519 g of $FeSO_4$.

Storage : Store in tightly-closed containers.

Ferrous Sulphate Tablets

Category : Haematinic.

Dose : Dried Ferrous Sulphate. Prophylactic, 200 mg daily; therapeutic, 400 mg to 600 mg daily, in divided doses.

Usual strength : 200 mg.

Standards : Ferrous Sulphate Tablets contain a quantity of $FeSO_4$ equivalent to not less than 80.0 per cent and not more than 90.0 per cent of the stated amount of Dried Ferrous Sulphate. The tablets are coated.

Identification : Dissolve a quantity of the powdered tablets equivalent to about 1 g of Dried Ferrous Sulphate in

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

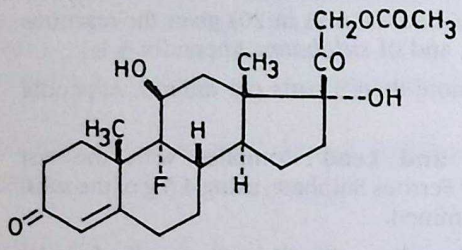
10 ml of *water* and filter, if necessary. The solution gives the reactions of *ferrous salts*, and of *sulphates*, Appendix 3.1.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately about 0.5 g of the powder and carry out the **Assay** described under Dried Ferrous Sulphate.

Storage : Store in tightly-closed containers.

Fludrocortisone Acetate



$C_{23}H_{31}FO_6$ Mol. Wt. 422.49

Category : Adrenocortical steroid (salt-regulating).

Dose : 1 to 2 mg in acute adrenocortical insufficiency; for maintenance, 0.1 to 0.2 mg, once a day.

Description : White or almost white, crystalline powder; odourless or almost odourless; hygroscopic.

Solubility : Practically insoluble in *water*; slightly soluble in *solvent ether*; sparingly soluble in *alcohol*, and in *chloroform*.

Standards : Fludrocortisone Acetate is 9α-fluoro-11β,17α,21-trihydroxypregn-4-ene-3, 20-dione 21-acetate (9α-fluorohydrocortisone 21-acetate). It contains not less than 96.0 per cent and not more than the equivalent of 104.0 per cent of $C_{23}H_{31}FO_6$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar intensities to, those in the spectrum of *fludrocortisone acetate R.S.*, Appendix 5.15B.

(B) To a warm 1 per cent w/v solution in *methyl alcohol*, add an equal volume of *potassium cupri-tartrate solution*, a red precipitate is produced.

(C) Complies with the test for *identification of steroids*, Appendix 3.3.11, using *solvent I* and *mobile phase B*.

Specific optical rotation : Between +148° and +156°, determined in 1 per cent w/v solution in *dioxan*, Appendix 5.12.

Light absorption : *Extinction* of a 1-cm layer of a 0.001 per cent w/v solution in *ethyl alcohol* at the maximum at about 240 nm, 0.39 to 0.42, Appendix 5.15 A.

Related foreign steroids : Complies with the test for *related foreign steroids, Method A*, Appendix 3.3.12.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Carry out the **Assay** described under Betamethasone, using *fludrocortisone acetate R.S.* for preparing the *standard solution*.

Storage : Store in well-closed, light-resistant containers.

Fludrocortisone Tablets

Category : Adrenocortical steroid (salt-regulating).

Dose : Fludrocortisone Acetate. In the treatment of acute adrenocortical insufficiency, 1 to 2 mg; maintenance dose, 0.1 to 0.2 mg daily.

Usual strength : 0.1 mg.

Standards : Fludrocortisone Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Fludrocortisone Acetate, $C_{23}H_{31}FO_6$.

Identification : Powder a few tablets and extract with *chloroform*. Evaporate the extract to dryness. The residue complies with the **identification** tests described under Fludrocortisone Acetate.

Uniformity of content : Powder one tablet, disperse in 10 ml of *water* and extract with three quantities, each of 5 ml, of *chloroform*. Filter the extracts through a plug of cotton wool moistened with *chloroform*. Evaporate the chloroform on a water-bath just to dryness. Cool and dissolve the residue on a 10.0 ml of *ethyl alcohol*. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 240 nm, Appendix 5.15 A. Calculate the content of $C_{23}H_{31}FO_6$, taking 405 as the value of E(1 per cent, 1-cm) at the maximum at about 240 nm.

Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 90 and 110 per cent of the average except that for one tablet the content may be between 85 and 115 per cent of the average.

Other requirements : Comply with the requirements stated under Tablets.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

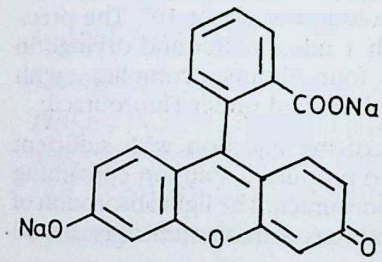
Digitized by Arya Samaj Foundation Chennai and eGangotri

Assay : Weigh and finely powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 1.0 mg of Fludrocortisone Acetate and transfer with the aid of 15 ml of *water* to a separator. Extract with four quantities, each of 15 ml, of *chloroform*, filtering each extract through *chloroform-washed* cotton into a 100-ml volumetric flask. Add *chloroform* to volume and mix. Transfer 20.0 ml of this solution to a glass-stoppered 50-ml flask, evaporate the *chloroform* on a water-bath just to dryness. Cool and dissolve the residue in 20.0 ml of *aldehyde-free ethyl alcohol* to give the *test solution*. Carry out the *assay of steroids*, Appendix 3.3.10, preparing the *standard solution*.

Storage : Store in well-closed, light-resistant containers.

Fluorescein Sodium

Soluble Fluorescein



$C_{20}H_{10}Na_2O_5$ Mol. Wt. 376.28

Category : Diagnostic aid (circulation time, corneal trauma indicator).

Dose : 0.5 to 1.25 g.

Description : Orange-red powder; odourless; almost tasteless; hygroscopic.

Solubility : Freely soluble in *water* and sparingly soluble in *alcohol*.

Standards : Fluorescein Sodium is the disodium salt of 9-(2-carboxyphenyl)-6-hydroxy-3*H*-xanthen-3-one. It contains not less than 98.5 per cent of $C_{20}H_{10}Na_2O_5$, calculated with reference to the dried substance.

Identification : (A) A solution is strongly fluorescent, even in extreme dilutions. The fluorescence disappears when the solution is made acidic, and reappears when it is made alkaline.

(B) The residue left after incineration gives the reactions of *sodium*, Appendix 3.1.

(C) A drop of a 0.05 per cent w/v solution, absorbed on a piece of filter paper, colours the paper yellow. On exposing the moist paper to the vapours of *bromine* for one minute and then to the vapours of ammonia, the yellow colour becomes deep pink.

Zinc : Dissolve 0.1 g in 10 ml of *water*, add 2 ml of *hydrochloric acid*, filter and add 0.1 ml of *potassium ferrocyanide solution*; no turbidity or precipitate is produced immediately.

Chloride : Dissolve 0.1 g in 20 ml of *water*, add 1 ml of *nitric acid* and filter; the filtrate complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphate : Dissolve 50 mg in 20 ml of *water*, and 2.5 ml of *dilute hydrochloric acid* and filter, the filtrate complies with the *limit test for sulphates*, Appendix 3.2.8.

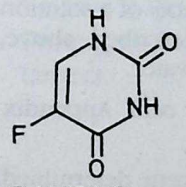
Acriflavin : Dissolve 10 mg in 5 ml of *water*, and add a few drops of *sodium salicylate solution*, no precipitate is formed.

Loss on drying : Not more than 10.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.5 g and dissolve in 20 ml of *water*, add 5 ml of *dilute hydrochloric acid*, and extract with four quantities, each of 20 ml, of a mixture of equal volumes of *isobutyl alcohol* and *chloroform*. Wash the combined extracts with 10 ml of *water*, extract the *water* with 5 ml of the mixture of *isobutyl alcohol* and *chloroform*, and add to the combined extracts. Evaporate the combined extracts to dryness on a water-bath in a current of air, dissolve the residue in 10 ml of alcohol, evaporate to dryness on a water-bath, and dry to constant weight at 105°. Each g of residue is equivalent to 1.132 g of $C_{20}H_{10}Na_2O_5$.

Storage : Store in well-closed containers.

Fluorouracil



$C_4H_3FN_2O_2$ Mol. Wt. 130.08

Category : Antineoplastic agent.

Dose : By intravenous injection, 3 mg per kg on alternate days to 12 mg per kg daily, to a maximum of 800 mg daily.

CAUTION—Great care should be taken to prevent inhaling particles of Fluorouracil and exposing the skin to it.

Description : White, or almost white, crystalline powder; practically odourless.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Solubility : Sparingly soluble in *water*, slightly soluble in *alcohol*; practically insoluble in *chloroform* and in *solvent ether*.

Standards : Fluorouracil is 5-fluoro-pyrimidine-2, 4 (1*H*, 3*H*)-dione. It contains not less than 98.5 per cent and not more than the equivalent of 101.0 per cent of $C_4H_3FN_2O_2$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* of a mineral oil dispersion, exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to those in the spectrum of *fluorouracil R.S.*, Appendix 5.15 B.

(B) The ultra-violet absorption spectrum in the range 230 to 350 nm of a 0.001 per cent w/v solution in *acetate buffer, pH 4.7* exhibits a maximum only at 266 nm, Appendix 5.15 A.

(C) To 5 ml of a 1 per cent w/v solution add 1 ml of *bromine water*; the bromine colour is discharged.

Heavy metals : Not more than 20 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

Fluorine content : Between 13.9 per cent and 15.0 per cent calculated with reference to the dried substance and determined by the following method: Burn 10 mg by the *oxygen-flask method*, Appendix 3.3.6, using 20 ml of *water* as the absorbing liquid. When the process is complete, add sufficient *water* to produce 100.0 ml. To 2.0 ml add 50 ml of *water*, 10 ml of *alizarin fluorine blue solution*, 3 ml of a solution containing 12 per cent w/v of *sodium acetate* and 6 per cent v/v of *glacial acetic acid*, 10 ml of *cerous nitrate solution*, and sufficient *water* to produce 100.0 ml. Allow to stand in the dark for one hour and measure the *extinction* of a 1-cm layer of the resulting solution at 610 nm, Appendix 5.15 A, using as the blank a solution prepared as described above beginning at the words "To 2.0 ml. . ." but using 2 ml of *water* instead of the solution. Calculate the content of fluorine from a reference curve prepared by treating suitable aliquots of a solution of *sodium fluoride* in the manner described above, beginning at the words "add 50 ml of water. . .".

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined or 1.0 g by drying "in vacuo at 80°" for four hours, Appendix 5.8.

Assay : Weigh accurately about 0.4 g, transfer to a 250-ml flask, add 80 ml of *dimethylformamide*, and warm gently to dissolve. Cool, add 5 drops of a 1 per cent w/v solution of *thymol blue* in *dimethyl formamide*, and titrate with *0.1N tetrabutylammonium hydroxide* in *methyl alcohol* to a blue end-point, taking precautions to prevent absorption of atmospheric carbon dioxide. Perform a blank determination and make any necessary correction. Each ml of *0.1N tetrabutylammonium hydroxide* is equivalent to 0.01301 g of $C_4H_3FN_2O_2$.

Storage : Store in tightly-closed, light-resistant containers.

Fluorouracil Injection

Category : Antineoplastic agent.

Dose : Fluorouracil. By intravenous injection, 3 mg per kg on alternate days to 12 mg per kg daily, to a maximum of 800 mg daily.

Usual strength : 50 mg in 1 ml.

Standards : Fluorouracil Injection is a sterile solution of Fluorouracil in Water for Injection, prepared with the aid of Sodium Hydroxide. It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of $C_4H_3FN_2O_2$.

Identification : (A) Acidify 2 ml with *glacial acetic acid*, stir and cool the solution to about 10°. The precipitate, after washing with 1 ml of *water* and drying "in vacuo at 80°" for four hours complies with **Identification** test (A) described under Fluorouracil.

(B) Dilute a volume of the injection with sufficient *acetate buffer, pH 4.7* to produce a solution containing 0.001 per cent w/v of Fluorouracil. The light absorption of the resulting solution exhibits a maximum only at 266 nm, Appendix 5.15 A.

(C) To a volume of the injection equivalent to 50 mg of Fluorouracil, add 1 ml of *bromine water*; the colour of bromine is discharged.

pH : Between 8.6 and 9.0, Appendix 5.10.

Pyrogens : Complies with the *test for pyrogens*, using 1 ml per kg of the rabbit's weight, of a suitable quantity of the injection diluted with *saline solution* to produce a solution containing 10 mg of Fluorouracil per ml, Appendix 2.36.

Other requirements : Complies with the requirements stated under Injections.

Assay : Dilute a volume equivalent to 0.1 g of Fluorouracil with sufficient *acetate buffer, pH 4.7* to produce 500.0 ml. Dilute 5.0 ml to 100.0 ml with *acetate buffer, pH 4.7* and measure the *extinction* of the resulting solution at the maximum about 266 nm, Appendix 5.15 A. Calculate the content of $C_4H_3FN_2O_2$, from the *extinction* obtained by repeating the **Assay,** using *fluorouracil R.S.* in place of the injection, and from the declared content of $C_4H_3FN_2O_2$ in the *fluorouracil R.S.*

Storage : Store in single-dose, light-resistant containers at controlled room temperature; it should not be allowed to freeze.

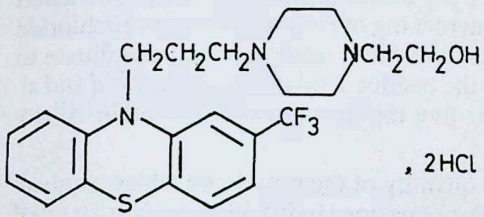
CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Labelling : The label on the container states (1) the date after which the injection is not intended to be used; (2) the storage conditions; (3) that if separation has occurred, the injection should be heated to 60°, vigorously shaken and allowed to cool to body temperature prior to use.

Fluphenazine Hydrochloride

Triflumethazine Hydrochloride



$C_{22}H_{26}F_3N_3OS, 2HCl$ Mol. Wt. 510.46

Category : Tranquilliser.

Dose : 1 to 2 mg daily in single or divided doses (in anxiety states). Upto 15 mg daily, in divided doses (for treatment of schizophrenia).

Description : White or almost white, crystalline powder; odourless.

Solubility : Freely soluble in *water*; slightly soluble in *acetone*, in *alcohol*, and in *chloroform*; practically insoluble in *benzene* and in *solvent ether*.

Standards : Fluphenazine Hydrochloride is dihydrochloride of 2-[4-{3-(2-trifluoromethyl-10-phenothiazinyl) propyl} piperazin-1-yl]ethanol. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_{22}H_{26}F_3N_3OS, 2HCl$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar intensities to those in the spectrum of *fluphenazine hydrochloride R.S.*, Appendix 5.15 B.

(B) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.001 per cent w/v solution in a mixture of 1 volume of *N hydrochloric acid* and 99 volumes of *alcohol (80 per cent)* exhibits a maximum at about 258 nm and a less well-defined maximum at 310 nm; *extinction* at 258 nm, about 0.6, Appendix 5.15 A.

(C) Dissolve 5 mg in 2 ml of *sulphuric acid* and allow to stand for five minutes; an orange colour is produced.

(D) A solution (1 in 10) gives the reactions of *chlorides*, Appendix 3.1.

pH : Between 1.9 and 2.3, determined in a 5.0 per cent w/v solution, Appendix 5.10.

Heavy metals : Not more than 40 parts per million, determined by Method B on 0.5 g, Appendix 3.2.4.

Foreign substances : Carry out in subdued light the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel GF 254* as the coating substance and a mixture of 80 volumes of *acetone*, 30 volumes of *cyclohexane* and 5 volumes of *strong ammonia solution* as the mobile phase. Apply separately to the plate 10µl of each of three solutions in *0.1N methanolic sodium hydroxide* containing (1) 1.0 per cent w/v of the substance being examined, (2) 0.01 per cent w/v of the substance being examined and (3) 0.005 per cent w/v of the substance being examined. After removal of the plate, allow to dry in air and examine under an ultra-violet lamp having a maximum output at about 254 nm. Any spot in the chromatogram obtained with solution (1), other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (3), except that any spot on the base-line and one other secondary spot, may not be more intense than the spot in chromatogram obtained with solution (2).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 100° to 105°, Appendix 5.8.

Assay : Weigh accurately about 0.6 g and dissolve in 30 ml of *glacial acetic acid*, warming slightly, if necessary, to effect solution. Cool, add 10 ml of *mercuric acetate solution*, two drops of *crystal-violet solution*, and titrate with *0.1N perchloric acid* to a green end-point. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02552 g of $C_{22}H_{26}F_3N_3OS, 2HCl$.

Storage : Store in well-closed, light-resistant containers.

Fluphenazine Hydrochloride Injection

Category : Tranquilliser.

Dose : Fluphenazine Hydrochloride, by intramuscular injection, 1.25 to 10 mg daily.

Usual strength : 2.5 mg per ml.

Description : Clear; colourless solution.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Standards : Fluphenazine Hydrochloride Injection is a sterile solution of Fluphenazine Hydrochloride in Water for Injection. It contains not less than 95.0 per cent and not more than 110.0 per cent of the stated amount of $C_{22}H_{26}F_3N_3OS$, 2HCl.

Identification : (A) To a volume equivalent to about 5 mg of Fluphenazine Hydrochloride, add 8 ml of *water*, and mix. Divide the solution into two 5-ml portions. To one portion add 5 ml of a mixture of equal volumes of *nitric acid* and *water*, and mix; an amber colour develops which turns dark brown, then suddenly changes to a clear yellow-coloured solution. To the other portion add 1 ml of *hydrochloric acid* and mix; the solution remains clear.

(B) Carry out in subdued light the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel GF 254* as the coating substance and a mixture of 40 parts of *benzene*, 10 volumes of *methyl alcohol* and 1 volume of *strong ammonia solution* as the mobile phase. Apply separately to the plate 10 µl of each of the following solutions: (1) To a volume equivalent to about 10 mg of Fluphenazine Hydrochloride add 25 ml of *sodium hydroxide solution* and extract with 20 ml of *iso-octane*. Evaporate the iso-octane solution to dryness and dissolve the residue in 0.5 ml of a mixture of 4 volumes of *methyl alcohol* and 1 volume of *water*. (2) To 10 mg of *fluphenazine hydrochloride R.S.* in a separator add 5 ml of *water* and 20 ml of *dilute hydrochloric acid* and shake for ten minutes; add 20 ml of chloroform-saturated 10 per cent w/v solution of *sodium carbonate* and shake with five successive quantities, each of 30 ml, of *chloroform*. Filter each extract through a plug of chloroform-washed cotton-wool. Evaporate the extracts on a water-bath to dryness and dissolve the residue in 0.5 ml of a mixture of 4 volumes of *methyl alcohol* and 1 volume of *water*. After removal of the plate allow it to dry in air and spray with a 40 per cent v/v solution of *sulphuric acid* in *methyl alcohol*. The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

pH : Between 4.8 and 5.2, Appendix 5.10.

Other requirements : Complies with the requirements stated under Injections.

Assay : To an accurately measured volume equivalent to about 0.13 g of Fluphenazine Hydrochloride, add 30 ml of *glacial acetic acid*. Add 10 ml of *mercuric acetate solution*, two drops of *crystal-violet solution* and titrate with *0.1N perchloric acid* to a green end-point. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02552 g of $C_{22}H_{26}F_3N_3OS$, 2HCl.

Storage : Store in single-dose or multi-dose, light-resistant containers.

Fluphenazine Tablets

Category : Tranquilliser.

Dose : Fluphenazine Hydrochloride, 1 to 2 mg daily, in single or divided doses (in anxiety states); upto 15 mg daily in divided doses (for treatment of schizophrenia).

Usual strengths : 1 mg; 2.5 mg; 5 mg.

Standards : Fluphenazine Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Fluphenazine Hydrochloride, $C_{22}H_{26}F_3N_3OS$, 2HCl. The tablets may be coated.

Identification : (A) Extract a quantity of the powdered tablets equivalent to 5 mg of Fluphenazine Hydrochloride with 5 ml of *acetone*, filter, and evaporate the filtrate to dryness. Add to the residue 2 ml of *sulphuric acid* and allow to stand for five minutes; an orange colour is produced.

(B) Extract a quantity of the powdered tablets equivalent to 7 mg of Fluphenazine Hydrochloride with 10 ml of *ethyl alcohol* containing 0.2 per cent v/v of *strong ammonia solution* and evaporate the extract to dryness. The residue complies with **Identification** test (C) described under Betamethasone.

Uniformity of content : Protect the solution from light throughout the test.

Powder one tablet and dissolve the powder as completely as possible in a mixture of 1 volume of *N hydrochloric acid* and 99 volumes of *alcohol (80 per cent)*. Add sufficient of the acid-alcohol mixture to produce 100.0 ml and filter. Pipette a volume of the filtrate equivalent to 0.5 mg of Fluphenazine Hydrochloride into a 100-ml graduated flask and make up to volume with the acid-alcohol mixture. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 258 nm, Appendix 5.15 A. Calculate the content of $C_{22}H_{26}F_3N_3OS$, 2HCl taking 620 as the value of E(1 per cent, 1-cm) at the maximum at about 258 nm.

Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 90 and 110 per cent of the average except that for one tablet the content may be between 85 and 115 per cent of the average.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Protect the solution from light throughout the assay.

Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 5 mg of Fluphenazine Hydrochloride and dissolve as completely as possible in a mixture of 1 volume of *N hydrochloric acid* and 99 volumes of *alcohol (80 per cent)*, add sufficient of the acid-alcohol mixture to produce 100.0 ml and filter. Dilute

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

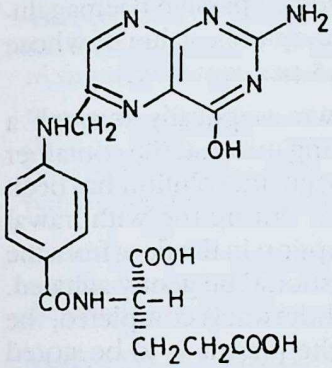
Digitized by Arya Samaj Foundation Chennai and eGangotri

10.0 ml of the filtrate to 100.0 ml with the acid-alcohol mixture and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 258 nm, Appendix 5.15 A. Calculate the content of $C_{22}H_{26}F_3N_3OS$, 2HCl, taking 620 as the value of E(1 per cent, 1-cm) at the maximum at about 258 nm.

Storage : Store in well-closed containers.

Folic Acid

Pteroylglutamic Acid



$C_{19}H_{19}N_7O_6$ Mol. Wt. 441.40

Category : Vitamin B (hematopoietic).

Dose : In the treatment of megaloblastic anaemia associated with folic acid deficiency, 5 to 20 mg daily. In the prophylaxis of megaloblastic anaemia of pregnancy, 0.2 to 0.5 mg daily.

Description : Yellow to yellowish-orange, crystalline powder; almost odourless and tasteless.

Solubility : Practically insoluble in cold *water*; very slightly soluble in boiling *water*; completely soluble in *N sodium hydroxide* giving a clear orange-brown solution which slowly deposits crystals on standing.

Standards : Folic Acid is 4-(2-amino-4-hydroxypteridin-6-yl) methylaminobenzoyl-L-glutamic acid. It contains not less than 95.0 per cent and not more than the equivalent of 102.0 per cent of $C_{19}H_{19}N_7O_6$, calculated with reference to the anhydrous substance.

Identification : The light absorption, in the range 230 to 380 nm of a 1-cm layer of a 0.001 per cent w/v solution in *0.1N sodium hydroxide* exhibits three maxima, at 256 nm, 283 nm and 365 nm, *extinction* at 256 nm, about 0.55, at 283 nm, about 0.55 and at 365 nm, about 0.185, Appendix 5.15 A. Ratio of the *extinction* at 256 nm to that at 365 nm, 2.8 to 3.0.

Specific optical rotation : About +20°, determined in a 1.0 per cent w/v solution in *0.1N sodium hydroxide*, Appendix 5.12.

Free amines : The *extinction* of the unreduced solution as determined in the **Assay** is not more than one-sixth of the *extinction* of the reduced solution.

Sulphated ash : Not more than 0.5 per cent, Appendix 3.2.7.

Water : Between 5.0 per cent and 8.5 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately about 0.05 g, dissolve in 50 ml of *0.1N sodium hydroxide* and add sufficient *0.1N sodium hydroxide* to produce 100.0 ml (solution A). To 3.0 ml add 20 ml of *2N hydrochloric acid* and dilute to 100.0 ml with *water*. To 50 ml add 0.5 g of *zinc powder*, allow to stand protected from light for twenty minutes with frequent shaking and filter. Dilute 10.0 ml of the filtrate to 25 ml with *water*, add 5 ml of *2N hydrochloric acid* and 5 ml of a 0.1 per cent w/v solution of *sodium nitrite*, mix and allow to stand for two minutes. Add 5 ml of a 0.5 per cent w/v solution of *ammonium sulphamate*, mix and allow to stand for two minutes. Add 5 ml of a 0.1 per cent w/v solution of *N-(1-naphthyl) ethylene diamine hydrochloride*, mix and allow to stand for ten minutes. Add sufficient *water* to produce 50.0 ml and measure the *extinction* of the resulting solution at about 550 nm, Appendix 5.15 A, using as the blank a solution prepared in a similar manner but using 25 ml of *water* and beginning at the words "add 5 ml of *2N hydrochloric acid*.....". To a further 30.0 ml of solution A add 20 ml of *2N hydrochloric acid* and sufficient *water* to produce 100.0 ml. Mix 10.0 ml of this solution with 15 ml of *water*, and carry out the operations described above, beginning at the words "add 5 ml of *2N hydrochloric acid*....". Subtract one-tenth of the *extinction* of the unreduced solution from that of the reduced solution and from the result calculate the amount of $C_{19}H_{19}N_7O_6$, using the result obtained by repeating the operation using *folic acid R.S.* instead of the substance being examined and the declared content of $C_{19}H_{19}N_7O_6$ in *folic acid R.S.*

Storage : Store in tightly-closed, light-resistant containers.

Folic Acid Tablets

Category : Vitamin B (hematopoietic).

Dose : Folic Acid. In the treatment of megaloblastic anaemia associated with folic acid deficiency, 5 to 20 mg daily.

In the prophylaxis of megaloblastic anaemia of pregnancy, 0.2 to 0.5 mg daily.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Usual strength : 5 mg.

Standards : Folic Acid Tablets contain not less than 90.0 per cent and not more than 115.0 per cent of the stated amount of Folic Acid, $C_{19}H_{19}N_7O_6$.

Identification : Dissolve a quantity of the powdered tablets equivalent to 5 mg of Folic Acid as completely as possible in 5 ml of *0.1N sodium hydroxide* and filter. To the filtrate add 45 ml of *0.5N hydrochloric acid* and 5 g of *zinc powder* and shake for thirty minutes. To 5 ml of the reduced solution, add 2 ml of a 0.1 per cent w/v solution of *sodium nitrite*, allow to stand for two minutes, add 2 ml of a 0.5 per cent w/v solution of *ammonium sulphamate*, allow to stand for three minutes and add 2 ml of a 0.1 per cent w/v solution of *N(1-naphthyl) ethylenediamine hydrochloride*; a deep magenta colour is produced.

Free amines : The *extinction* of the unreduced solution as determined in the **Assay,** is not more than one-third of the *extinction* of the reduced solution.

Uniformity of content : Crush one tablet, add 10.0 ml of *0.1N sodium hydroxide*, shake for ten minutes and centrifuge. Using 3.0 ml of the supernatant liquid complete the **Assay** described under Folic Acid, beginning at the words "add 20 ml of *2N hydrochloric acid* .....". Calculate the content of $C_{19}H_{19}N_7O_6$. Repeat the operation using a further nine tablets and calculate the average content of the tablets.

The content of each tablet is between 85 per cent and 115 per cent of the average except that for one tablet the content may be between 80 per cent and 120 per cent of the average.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and finely powder 20 tablets or more, if necessary. Weigh accurately a quantity of the powder equivalent to about 50 mg of Folic Acid, shake with 50 ml of *0.1N sodium hydroxide*, filter and dilute to 100.0 ml with *0.1N sodium hydroxide*. Complete the **Assay** described under Folic Acid, beginning at the words "To 3.0 ml add 20 ml of *2N hydrochloric acid*.....".

Storage : Store in well-closed, light-resistant containers.

Dried Human Antihaemophilic Fraction

Category : Antihaemophilic.

Description : White powder or friable solid.

Standards : Dried Human Antihaemophilic Fraction is a preparation of antihaemophilic factor, which is obtained from a single unit of plasma collected and processed in a closed system; it is rich in clotting factor VIII.

Blood to be used for preparing Dried Human Antihaemophilic Fraction is obtained from human subjects (a) who are, as far as can be ascertained by a registered medical practitioner after simple clinical examination and consideration of their medical history, free from disease transmissible by blood transfusion, (b) whose blood has been tested with negative results for evidence of syphilitic infection, (c) whose blood has been tested with negative results for the presence of hepatitis B antigen by a method not less sensitive than reversed passive haemagglutination, and (d) the haemoglobin value of whose blood is not less than 12.5 per cent w/v.

The blood is withdrawn aseptically through a closed sytem of sterile tubing into a sterile container in which a suitable anticoagulant solution has been placed before sterilisation. During the withdrawal there should be no interruption in the flow from the donor and the container should be gently agitated. Immediately after the withdrawal is completed, the blood is cooled at 4°; if the plasma is to be stored frozen it should be separated from cellular components by centrifugation and frozen to −30° or below, preferably within twelve hours of collection; if the plasma is not be frozen it should be separated from cellular components by centrifugation as soon as possible and not later than eighteen hours after collection, and fractionation begun without delay.

Dried Human Antihaemophilic Fraction may be prepared from human plasma so obtained by precipitation under controlled conditions of pH, ionic strength and temperature with organic solvents, or by freezing and thawing. The precipitate may be washed by extraction with suitable solvents dissolved in a solution of Sodium Citrate adjusted to a pH of 6.8 to 7.2, which may also contain Sodium Chloride. The solution is sterilised by filtration through a membrane filter, distributed in sterile containers, and dried from the frozen state. The air is removed or replaced by *oxygen-free nitrogen* and the containers are sealed. No preservative is added. When the contents of a sealed container are dissolved in a volume of *water* equal to the volume of Water for Injection stated on the label, the resulting solution contains not less than 3.0 Units per ml and not less than 0.1 Unit per mg of protein of which not more than 80 per cent is fibrinogen and not more than 200 millimoles of sodium ions per litre.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Identification : (A) By precipitation tests with specific antisera, contains plasma proteins of human origin.

(B) A freshly prepared solution in *water* has the property of correcting the clotting abnormality in plasma deficient in clotting factor VIII.

Solubility : Slowly add a volume of *water* at 20°, indicated on the label to the contents of sealed container, also at 20°. Mix gently by rotation, avoiding frothing; the substance dissolves completely within thirty minutes forming a clear or slightly opalescent solution.

Loss on drying : Not more than 0.5 per cent, determined by drying "in vacuo" for twenty-four hours, Appendix 5.8.

Sterility : Complies with the *tests for sterility*, Appendix 4.6. Reconstitute the contents of the sealed container with the requisite amount of *sterile water for injection*. The reconstituted solution complies with the following tests:

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using a volume equivalent to not less than 10 Units per kg of the rabbit's weight, and rabbits that have not previously received blood products.

Undue toxicity : Complies with the *test for Undue toxicity for vaccines and sera*, Appendix 2.37, using 0.5 ml of the solution for each mouse and 5 ml for each guinea-pig.

Assay : (1) *For potency*—Carry out the *biological assay of human antihaemophilic fraction*, Appendix 2.2. The estimated potency is not less than 80 per cent and not more than 120 per cent of the stated potency. The fiducial limits of error are not less than 60 per cent and not more than 140 per cent of the stated potency.

(2) *For total protein*—Dilute 1.0 ml to 10.0 ml with *saline solution*. Carry out the **Assay** described under Human Plasma, using 5.0 ml of the dilution and beginning at the words "add 0.2 ml of a 7.5 per cent w/v solution.....".

(3) *For fibrinogen*—Dilute 1.0 ml to 10.0 ml with a phosphate-saline buffer at pH 6.5 and ionic strength 0.15. Clot 5.0 ml of the dilution with the minimum amount of thrombin, collect the clot and complete the **Assay** described under Human Plasma, beginning at the words "add three drops of a 30 per cent w/v solution.....". Each ml of *0.02N hydrochloric acid* is equivalent to 0.00175 g of fibrinogen.

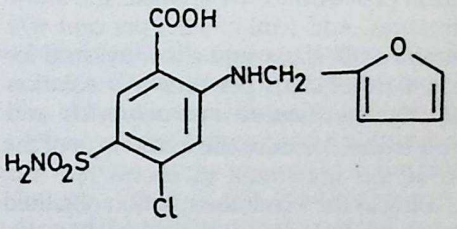
(4) *For sodium ions*—To 10.0 ml add sufficient *water* to produce 100.0 ml, dilute 10.0 ml to 500.0 ml with *water* and determine by Method B for *flame photometry*, Appendix 5.16 A, measuring at 589 nm and using *sodium solution FP* suitably diluted with *water* as the standard solution.

Storage : Store in an atmosphere of nitrogen of "in vacuo" in a sterile container sealed so as to exclude micro-organisms, protected from light and moisture and at a temperature below 6°.

Labelling : The label on the container states (1) the ABO blood group designation of the source of blood; (2) the number of Units contained in it; (3) that one Unit is approximately equivalent to the antihaemophilic activity of 1 ml of average normal plasma; (4) the concentration of protein in g per litre and of sodium ions in millimoles per litre; (5) the name and amount of any other added substance contained in it; (6) that the preparation must be allowed to warm to 20° to 30° before reconstitution; (7) the volume of Water for Injection necessary to reconstitute the solution; (8) instructions for reconstitution and that reconstitution may take upto thirty minutes; (9) that if a gel forms on reconstitution, the preparation should not be used; (10) that the preparation is of human origin and cannot be assumed to be free of hepatitis virus; (11) that the solution should be used as soon as possible and in any case within three hours of reconstitution; (12) the storage condition; (13) the date after which the contents are not intended to be used.

Frusemide

Furosemide



$C_{12}H_{11}ClN_2O_5S$ Mol. Wt. 330. 74

Category : Diuretic.

Dose : 40 to 120 mg daily.

Description : White or almost white, crystalline powder; odourless; almost tasteless.

Solubility : Practically insoluble in *water* and in *chloroform*; slightly soluble in *alcohol* and in *solvent ether*, soluble in *acetone* and in solutions of alkali hydroxides.

Standards : Frusemide is 4-chloro-*N*-furfuryl-5-sulphamoylanthranilic acid. It contains not less than 98.0 per cent and not more than 101.0 per cent of $C_{12}H_{11}ClN_2O_5S$, calculated with reference to the dried substance.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Identification : (A) The light-absorption, in the range 220 to 350 nm, of a 1-cm layer of a 0.001 per cent w/v solution in *0.1N sodium hydroxide* exhibits maxima at 228 nm and 271 nm; *extinction* at 228 nm, about 1.06 and at 271 nm, about 0.58, Appendix 5.15 A.

(B) Dissolve 25 mg in *alcohol* and add 2 ml of *dimethylaminobenzaldehyde solution*; a green colour is produced which becomes deep red.

(C) Dissolve 5 mg in 10 ml of *methyl alcohol*. Transfer 1 ml to a flask, add 10 ml of *dilute hydrochloric acid* and boil under a reflux condenser on a water-bath for fifteen minutes. Cool, add 15 ml of *N sodium hydroxide* and 5 ml of a 0.1 per cent w/v solution of *sodium nitrite*. Allow to stand for three minutes add 5 ml of a 0.5 per cent solution of *ammonium sulphamate*, mix and add 5 ml of a 0.1 per cent solution of *N-(1-naphthyl) ethylenediamine hydrochloride*; a red-violet colour is produced.

(D) Dissolve 25 mg in 2.5 ml of *alcohol* and add 5 ml of *water*, the solution turns *blue litmus paper* red.

(E) It melts at about 208° with decomposition, Appendix 5.11.

Heavy metals : Not more than 20 parts per million, determined on 1 g by Method B, Appendix 3.2.4.

Chloride : Shake 1.0 g with 40 ml of *water* for five minutes and filter, the filtrate complies with the *limit test for chlorides*, Appendix 3.2.2.

Free amine : Dissolve 0.10 g in 25 ml of *methyl alcohol*. To 1 ml add 3 ml of *dimethylformamide*, 12 ml of *water* and 1 ml of *N hydrochloric acid*. Cool, add 1 ml of a 0.5 per cent w/v solution of *sodium nitrite*, shake and allow to stand for five minutes. Add 1 ml of a 2.5 per cent w/v solution of *sulphamic acid*, shake and allow to stand for three minutes. Add 1 ml of a 0.5 per cent w/v solution of *N-(1-naphthyl)ethylenediamine hydrochloride* and dilute to 25 ml with *water*. Measure the *extinction* of the resulting solution at the maximum at about 530 nm, Appendix 5.15 A, using as the blank the solution obtained by treating 1 ml of *methyl alcohol* and 3 ml of *dimethyl formamide* in a similar manner; the *extinction* is not more than 0.12.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.5 g, dissolve in 40 ml of *dimethylformamide* and titrate with *0.1N sodium hydroxide*, using *bromothymol blue solution* as indicator. Repeat the operation without the substance being examined. The difference in titration represents the amount of sodium hydroxide required by Frusemide. Each ml of *0.1N sodium hydroxide* is equivalent to 0.03308 g of $C_{12}H_{11}ClN_2O_5S$.

Storage : Store in well-closed, light-resistant containers.

Frusemide Injection

Furosemide Injection

Category : Diuretic.

Dose : Frusemide, by intramuscular or intravenous injection, 20 to 40 mg.

Usual strength : 10 mg per ml.

Description : Clear, colourless or almost colourless solution.

Standards : Frusemide Injection is a sterile solution of Frusemide in Water for Injection, prepared with the aid of Sodium Hydroxide. It contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of $C_{12}H_{11}ClN_2O_5S$.

Identification : (A) To a volume equivalent to 0.5 mg of Frusemide, add 10 ml of *dilute hydrochloric acid* and boil under a reflux condenser on a water-bath for fifteen minutes. Cool, add 15 ml of *N sodium hydroxide* and 5 ml of a 0.1 per cent w/v solution of *sodium nitrite*. Allow to stand for three minutes, add 5 ml of a 0.5 per cent solution of *ammonium sulphamate* and mix; add 5 ml of a 0.1 per cent solution of *N-(1-naphthyl) ethylenediamine hydrochloride*; a red-violet colour is produced.

(B) The light absorption of the final solution obtained in the **Assay**, in the range of 220 to 350 nm, exhibits a maxima at 228 nm and 271 nm, Appendix 5.15 A.

pH : Between 8.7 and 9.3, Appendix 5.10.

Free amine : To a volume equivalent to 4 mg of Frusemide, add 3 ml of *dimethylformamide*, 12.5 ml of *water*, and 1 ml of *N hydrochloric acid*. Complete the test described under Frusemide, commencing with the words "Cool, add 1 ml of a 0.5 per cent w/v solution.....".

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36 using a volume equivalent to 2 mg of Frusemide, diluted to not more than 5 ml with *water for injection*, per kg of the rabbit's weight.

Other requirements : Complies with the requirements stated under Injections.

Assay : Dilute an accurately measured volume equivalent to about 40 mg of Frusemide, with *water* to produce 100.0 ml. Dilute 1.0 ml of this solution with sufficient *0.1N sodium hydroxide* to produce 100.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 271 nm, Appendix 5.15 A. Calculate the content of $C_{12}H_{11}ClN_2O_5S$, taking 572 as the value of E(1 per cent, 1-cm) at the maximum at about 271 nm.

Storage : Store in light-resistant containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Frusemide Tablets

Furosemide Tablets

Category : Diuretic.

Dose : Frusemide 40 to 120 mg daily.

Usual strength : 40 mg.

Standards : Frusemide Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Frusemide. $C_{12}H_{11}ClN_2O_5S$.

Identification : Shake a quantity of the powdered tablets equivalent to about 80 mg of Frusemide with 10 ml of *alcohol*, filter and evaporate the filtrate to dryness, the residue complies with **Identification** tests (A), (B) and (C) described under Frusemide.

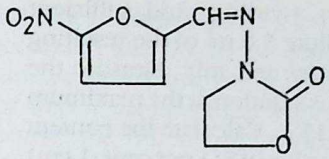
Free amine : Carry out in subdued light the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel HF 254* as the coating substance and a mixture of 1 volume of *toluene*, 1 volume of *xylene*, 3 volumes of peroxide-free *dioxan*, 3 volumes of *isopropyl alcohol*, and 2 volumes of *strong ammonia solution* as the mobile phase. Apply separately to the plate 5 µl of each of the following two solutions. For solution (1) shake a quantity of the powdered tablets equivalent to 40 mg of Frusemide with 25 ml of *acetone* for ten minutes, filter, evaporate the filtrate to dryness and dissolve the residue in 2 ml of *acetone*. Solution (2) is a 0.016 per cent w/v solution of *4-chloro-5-sulphamoylanthranilic acid R.S.* in *acetone*. After removal of the plate, dry in a current of air, and examine under an ultra-violet lamp having a maximum output at about 254 nm. The spot in the chromatogram obtained with solution (2) is more intense than any corresponding spot in the chromatogram obtained with solution (1).

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.2 g of Frusemide and shake with 300 ml of *0.1N sodium hydroxide* for ten minutes. Add sufficient *0.1N sodium hydroxide* to produce 500.0 ml and filter. Dilute 5.0 ml to 500.0 ml with *0.1N sodium hydroxide* and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 271 nm, Appendix 5.15 A. Calculate the content of $C_{12}H_{11}ClN_2O_5S$, taking 580 as the value of E(1 per cent, 1-cm) at the maximum at about 271 nm.

Storage : Store in well-closed, light-resistant containers.

Furazolidone



$C_8H_7N_3O_5$ Mol. Wt. 225.16

Category : Antibacterial and antiprotozoal.

Dose : 400 mg daily, in divided doses.

Description : Yellow, crystalline powder; odourless.

Solubility : Very slightly soluble in *water* and in *alcohol*; slightly soluble in *chloroform*; insoluble in *solvent ether*.

Standards : Furazolidone is 3-(5-nitrofurfurylideneamino)oxazolidin-2-one. It contains not less than 97.0 per cent and not more than the equivalent of 103.0 per cent of $C_8H_7N_3O_5$, calculated with reference to the dried substance.

Identification : Dissolve 1 mg in 1 ml of *dimethylformamide* and add 0.05 ml of *N alcoholic potassium hydroxide*; a deep blue colour is produced.

pH : Between 4.5 and 7.0, determined in a solution obtained by shaking 1.0 g for fifteen minutes with 100 ml of *carbon dioxide-free water* and filtering, Appendix 5.10.

Nitrofurfural diacetate : Carry out in subdued light the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 95 volumes of *toluene* and 5 volumes of *dioxan*, as the mobile phase. Apply separately to the plate the following solutions : (1) 20 µl of a solution prepared by dissolving 0.05 g of the substance being tested in 5 ml of *dimethylformamide* by heating on a water-bath for a few minutes, allowing to cool and diluting to 10 ml with *acetone* and (2) 10 µl of a 0.01 per cent w/v solution of *nitrofurfural diacetate R.S.* in a mixture of equal volumes of *dimethylformamide* and *acetone*. After removal of the plate, heat it at 105° for five minutes and spray with a solution prepared by dissolving 0.75 g of *phenylhydrazine hydrochloride* in 10 ml of *alcohol*, diluting to 50 ml with *water*, adding *decolorising charcoal*, filtering, and then adding 25 ml of *hydrochloric acid* and sufficient *water* to produce 200 ml. The spot in the chromatogram obtained with solution (2) is more intense than any corresponding spot in the chromatogram with solution (1).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 100° to 105°, Appendix 5.8.

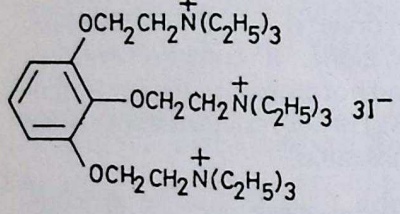
CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Assay : Protect the solution from light throughout the Assay. Weigh accurately about 0.08 g and dissolve in 150 ml of *dimethylformamide* by swirling. Add sufficient *water* to produce 500.0 ml. Dilute 5.0 ml of the resulting solution to 100.0 ml with *water* and mix. Measure the *extinction* of a 1-cm layer of this solution at the maximum at about 367 nm, Appendix 5.15 A. Calculate the content of $C_8H_7N_3O_5$, taking 750 as the value of E(1 per cent, 1-cm) at the maximum at about 367 nm.

Storage : Store in well-closed, light-resistant containers.

Gallamine Triethiodide



$C_{30}H_{60}I_3N_3O_3$ Mol. Wt. 891.54

Category : Muscle relaxant.

Dose : The dose is determined by the physician in accordance with the needs of the patient.

Description : White or faintly cream-coloured powder; odourless or with a slight odour; taste, slightly bitter. Hygroscopic.

Solubility : Very soluble in *water* and slightly soluble in *alcohol*.

Standards : Gallamine Triethiodide is [2,2′,2″-(1, 2,3-benzenetriyltrioxy) triethyl] tris-(triethylammonium iodide). It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_{30}H_{60}I_3N_3O_3$, calculated with reference to the dried substance.

Identification : (A) Dissolve 0.5 g in 50 ml of *alcohol*, warming if necessary. Add 10 ml of a 1.2 per cent w/v solution of *picric acid* in *alcohol*. Cool and filter. Recrystallize the residue from warm *alcohol*, filter and wash with *alcohol* and then with *solvent ether*; the melting-range of the residue after drying at 50° is between 83° and 87°, Appendix 5.11.

(B) To 5 ml of a 1 per cent w/v solution add 1 ml of *potassium mercuri-iodide solution*; a yellow precipitate is produced.

(C) The light absorption, in the range 220 to 350 nm, of a 0.001 per cent w/v solution in *0.01N hydrochloric acid* exhibits a maximum only at 225 nm, Appendix 5.15 A.

pH : Between 5.5 and 7.0, determined in a 4.0 per cent w/v solution, Appendix 5.10.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 5.0 per cent, determined on 1.0 g by drying "in vacuo at 60°", Appendix 5.8.

Iodine content : Between 41.4 per cent and 44.0 per cent, determined by the following method: Weigh accurately about 0.1 g and dissolve in 25 ml of *water*. Add 25 ml of *potassium permanganate solution* and 40 ml of *dilute sulphuric acid* and boil for five minutes. Cool, add *sodium nitrite solution*, dropwise, until the solution becomes clear and colourless. Add 3 g of *urea* and 2 g of *tartaric acid*. After ten minutes add 5 ml of *potassium iodide solution* and titrate with *0.1N sodium thiosulphate*. Each ml of *0.1N sodium thiosulphate* is equivalent to 0.002115 g of I.

Assay : Weigh accurately about 0.5 g and dissolve in a mixture of 40 ml of *acetone* and 15 ml of *mercuric acetate solution*. Titrate with *0.1N perchloric acid*, determining the end-point potentiometrically. Carry out a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02972 g of $C_{30}H_{60}I_3N_3O_3$.

Storage : Store in well-closed, light-resistant containers.

Gallamine Injection

Gallamine Triethiodide Injection

Category : Muscle relaxant.

Dose : Gallamine Triethiodide. By intravenous injection, 1 mg per kg of body weight, not exceeding 100 mg per dose, repeated at 30 to 45-minutes intervals if necessary.

Usual strength : 40 mg per ml.

Description : Clear, colourless or almost colourless solution.

Standards : Gallamine Injection is a sterile solution of Gallamine Triethiodide in Water for Injection containing Sodium Metabisulphite equivalent to not more than 0.1 per cent w/v of sulphur dioxide. It contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of $C_{30}H_{60}I_3N_3O_3$.

Identification : (A) To 1 ml add 1 ml of *0.1N iodine*; a brown precipitate is produced.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

(B) The residue obtained on evaporating 5 ml to dryness complies with **Identification** tests (A) and (B) described under Gallamine Triethiodide.

pH : Between 5.5 and 7.5, Appendix 5.10.

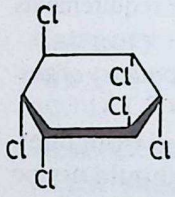
Other requirements : Complies with the requirements stated under Injections.

Assay : Dilute a volume equivalent to 40 mg of Gallamine Triethiodide with sufficient *0.01N hydrochloric acid* to produce 250.0 ml. Dilute 5.0 ml of this solution to 100.0 ml with *0.01N hydrochloric acid* and measure the *extinction* of the resulting solution at the maximum at about 225 nm, Appendix 5.15 A. Calculate the content of $C_{30}H_{60}I_3N_3O_3$, taking 525 as the value of E(1 per cent, 1-cm) at the maximum at about 225 nm.

Storage : Store in single-dose or multiple-dose, light-resistant containers.

Gamma Benzene Hexachloride

Benzene Hexachloride; Lindane



$C_6H_6Cl_6$ Mol. Wt. 290.83

Category : Pediculicide; cabicide.

Description : White, crystalline powder; odour, slight, musty.

Solubility : Practically insoluble in *water*; freely soluble in *chloroform* and in *acetone*; soluble in *ethyl alcohol*; sparingly soluble in *solvent ether*.

Standards : Gamma Benzene Hexachloride is 1α, 2α, 3β, 4α, 5α, 6β-hexachlorocyclohexane. It contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of $C_6H_6Cl_6$.

Identification : (A) Place a few mg on a clean copper wire, and gently ignite by heating it above the non-luminous flame of a Bunsen burner. Hold the wire in the flame after ignition is complete; a bright green colour is imparted to the flame.

(B) To 1 ml of 0.5 per cent w/v solution in *alcohol* in a stoppered cylinder, add 3 ml of *alcohol* and 1 ml of *alcoholic potassium hydroxide solution* and allow to stand for ten minutes; the solution gives the reactions of *chlorides*, Appendix 3.1.

Congealing temperature : Not less than 112°, Appendix 5.5.

Acidity : Dissolve 10 g in 25 ml of *acetone*, warming if necessary, add 75 ml of *water*, and titrate with *0.02N sodium hydroxide*, using *methyl red solution* as indicator. Repeat the operation without the substance being examined; the difference between the titrations does not exceed 13.7 ml.

Chloride ion : Shake 0.1 g with 10 ml of *water*, and filter. To the filtrate add 1 ml of *nitric acid* and 3 ml of *silver nitrate solution*; no turbidity is produced.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Water : Not more than 0.5 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately about 0.4 g, add 25 ml of *alcohol* and warm on a water-bath until dissolved. Cool, add 10 ml of *N alcoholic potassium hydroxide*, swirl gently, and allow to stand for ten minutes. Dilute to 150 ml with *water*, neutralise with *2N nitric acid*, and add 10 ml in excess, followed by 50.0 ml of *0.1N silver nitrate*. Filter, wash the residue with *water*, and titrate the combined filtrate and washings with *0.1N ammonium thiocyanate* using *ferric ammonium sulphate solution* as indicator. Perform a blank determination with the same quantities of reagents. Each ml of *0.1N silver nitrate* is equivalent to 0.009694 g of $C_6H_6Cl_6$.

Storage : Store in well-closed containers.

Gas-gangrene Antitoxin (Oedematiens)

Anti-gas-gangrene (Oedematiens) Serum

Category : Immunising agent.

Dose : By intravenous or intramuscular injection, prophylactic 10,000 International Units; therapeutic, not less than 30,000 International Units.

Description : Almost colourless or very faintly yellow liquid, free from turbidity.

Standards : Gas-gangrene Antitoxin (Oedematiens) is a preparation containing the specific antitoxic globulins obtained by purification from native serum and having the specific power of neutralising the α-toxin formed by *Clostridium oedematiens*.

It has a potency of not less than 3750 International Units per ml.

Identification : It specifically neutralises and renders the α-toxin formed by *Clostridium oedematiens* harmless to susceptible animals.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Other requirements : Complies with the requirements for general tests stated under Antisera.

Potency : Carry out the *determination of potency of gas-gangrene antitoxin (oedematiens)*, Appendix 2.15.

Storage : Store in containers, protected from light, at a temperature between 2° and 8°. It should not be allowed to freeze.

Labelling : The label on the container states (1) the number of Units per ml; (2) the storage conditions; (3) the date after which it is not intended to be used.

Gas-gangrene Antitoxin (Perfringens)

Anti-gas-gangrene (Perfringens) Serum

Category : Immunising agent.

Dose : By intravenous or intramuscular injection, prophylactic, 10,000 International Units; therapeutic, not less than 30,000 International Units.

Description : Almost colourless or very faintly yellow liquid, free from turbidity.

Standards : Gas-gangrene Antitoxin (Perfringens) is a preparation containing the specific antitoxic globulins obtained by purification from native serum and having the specific-power of neutralising the α-toxin formed by *Clostridium perfringens*.

It has a potency of not less than 1500 International Units per ml.

Identification : It specifically neutralises and renders the α-toxin formed by *Clostridium perfringens* harmless to susceptible animals.

Other requirements : Complies with the requirements for general tests stated under Antisera.

Potency : Carry out the *determination of potency of gas-gangrene antitoxin (perfringens)*, Appendix 2.16.

Storage : Store in containers, protected from light, at a temperature between 2° and 8°. It should not be allowed to freeze.

Labelling : The label on the container states (1) the number of Units per ml; (2) the storage conditions; (3) the date after which it is not intended to be used.

Gas-gangrene Antitoxin (Septicum)

Anti-gas-gangrene (Septicum) Serum

Category : Immunising agent.

Dose : By intravenous or intramuscular injection, prophylactic, 5,000 International Units; therapeutic, not less than 15,000 International Units.

Description : Almost colourless or very faintly yellow liquid, free from turbidity.

Standards : Gas-gangrene Antitoxin (Septicum) is a preparation containing the specific antitoxic globulins by purification from native serum and having the specific power of neutralising the α-toxin formed by *Clostridium septicum*, also known as *Vibrion septique*.

It has a potency of not less than 1500 International Units per ml.

Identification : It specifically neutralises and renders the α-toxin formed by *Clostridium septicum* harmless to susceptible animals.

Other requirements : Complies with the requirements for general tests stated under Antisera.

Potency : Carry out the *determination of potency of gas-ganigrene antitoxin (septicum)*, Appendix 2.17.

Storage : Store in containers, protected from light, at a temperature between 2° and 8°. It should not be allowed to freeze.

Labelling : The label on the container states (1) the number of Units per ml; (2) the storage conditions; (3) the date after which it is not intended to be used.

Mixed Gas-gangrene Antitoxin

Category : Immunising agent.

Dose : By intravenous or intramuscular injection, prophylactic, 25,000 International Units; therapeutic, not less than 75,000 International Units.

Description : Almost colourless or very faintly yellow liquid, free from turbidity.

Standards : Mixed Gas-gangrene Antitoxin is prepared by mixing Gas-gangrene Antitoxin (Oedematiens), Gas-gangrene Antitoxin (Perfringens) and Gas-gangrene (Septicum) in appropriate quantities.

It has a potency of not less than 1000 International Units of Gas-gangrene (Oedematiens), not

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

208/DGHS/NDI/90—5,000 F-17

less than 1000 International Units of Gas-gangrene (Perfringens) and not less than 500 International Units of Gas-gangrene (Septicum) per ml.

Identification : It specifically neutralises and renders the α-toxins formed by *Clostridium oedematiens*, *Clostridium perfringens* and *Clostridium septicum* harmless to susceptible animals.

Other requirements : Complies with the requirements for general tests stated under Antisera.

Potency : Carry out the determination of potency of each component, Appendices 2.15, 2.16, and 2.17.

Storage : Store in containers, protected from light, at a temperature between 2° and 8° It should not be allowed to freeze.

Labelling : The label on the container states (1) the number of Units of each component per ml; (2) the storage conditions; (3) the date after which it is not intended to be used.

Gelatin

Category : Pharmaceutical aid (encapsulating agent; suspending agent; tablet binder and coating agent).

Description : Colourless or pale yellowish, translucent sheets, flakes, shreds or a coarse to fine powder; odour and taste, very slight. Stable in air when dry but is subject to microbial decomposition when moist or in solution.

Solubility : Practically insoluble in cold *water*, but swells and softens when immersed in it, gradually absorbing from 5 to 10 times its own weight; soluble in hot *water*; practically insoluble in *alcohol*, in *chloroform*, and in *solvent ether*; soluble in a hot mixture of *glycerin* and *water*, and in *acetic acid*.

Standards : Gelatin is a product obtained by the partial hydrolysis of collagen, derived from the skin, white connective tissue, and bones of animals. Gelatin used in the manufacture of capsules or for the coating of tablets may contain suitable antimicrobial agents.

Identification : (A) A dilute aqueous solution yields a precipitate with *picric acid solution*, and with *tannic acid solution*, but not with other acids, and not with a dilute solution of *alum*, *lead acetate solution*, or *ferric chloride test solution*.

(B) Heat with *soda lime*; ammonia is evolved.

Odour and water-insoluble substances : A 2.5 per cent w/v hot solution is free from any unpleasant odour and on cooling is only slightly opalescent when viewed in a layer 2-cm thick.

Arsenic : Not more than 2 parts per million, Appendix 3.2.1.

Heavy metals : Not more than 50 parts per million, determined by Method A, Appendix 3.2.4, in a solution prepared in the following manner. To the residue obtained in the test for **Ash** add 2 ml of *hydrochloric acid* and 0.5 ml of *nitric acid*, and evaporate to dryness. To the residue add 1 ml of *N hydrochloric acid* and 15 ml of *water*, and warm for a few minutes. Filter, and wash with *water* to make the filtrate measure 100 ml. Dilute 8 ml of the resulting solution to 25 ml with *water*.

Copper : Not more than 30 parts per million, determined by the following method: Ignite 1.0 g in a silica basin at a temperature not exceeding 450° until completely ashed. Dissolve the residue in 1 ml of *dilute nitric acid*, dilute to 10 ml with *water*, add *dilute ammonia solution* until the solution is neutral to *litmus paper*, make faintly acid by the addition of *dilute acetic acid*, and add 0.25 ml of *ammonium acetate solution* and 2 drops of *potassium ferrocyanide solution*; any colour produced is not darker than that produced by treating a mixture of 7 ml of *water* and 3 ml of *dilute copper sulphate solution* in a similar manner.

Zinc : Not more than 100 parts per million, determined by the following methods: Ignite 1.0 g in a silica basin at a temperature not exceeding 450° until completely ashed. Dissolve the residue in 1 ml of *dilute nitric acid* and dilute to 10 ml with *water*; add *dilute ammonia solution* until the solution is neutral to *litmus paper*, add 2 ml of *dilute hydrochloric acid* and 2.5 g of *ammonium chloride*, dilute to 50 ml with *water* in a *Nessler cylinder*, and add 2 ml of a 20 per cent w/v solution of *sodium sulphite* and 2 drops of *potassium ferrocyanide solution*; any opalescence produced is not greater than that produced by treating a mixture of 6 ml of *water* and 4 ml of *dilute zinc sulphate solution* in a similar manner.

Microbial limits : Total bacterial count, not more than 1000 per g; 1 g meets the requirements of the test for the absence of *E. coil*, and 10 g is free from salmonellae, Appendix 4.5.

Ash : Not more than 3.25 per cent, determined by the following method: Weigh accurately 5.0 g, add about 2 g of paraffin (to avoid loss due to swelling) and incinerate at a temperature not exceeding 500° until free from carbon. Cool and weigh.

Loss on drying : Not more than 16.0 per cent, determined by the following method: Weigh accurately about 1 g and place in a stainless steel dish with an aluminium cover. The dish should weigh about 25 g and should have diameter of 70 mm and a height of 15 mm. Add 10 ml of *water* and allow to soak. Heat on a water-bath to form a homogenous solution and continue heating until most of

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

the water has evaporated. Dry for two hours at 105° and for further periods of thirty minutes until two successive weighings do not differ by more than 1 mg. (Do not powder sheet gelatin while preparing for this test).

Storage : Store in well-closed containers, in a dry place.

Gentamicin Sulphate

Category : Antibacterial.

Dose : By intramuscular injection 80 to 240 mg of gentamicin (80,000 to 240,000 Units) daily, in divided doses.

Description : White to cream-coloured powder.

Solubility : Freely soluble in *water*; soluble in *alcohol*, in *chloroform*, and in *solvent ether*.

Standards : Gentamicin Sulphate is a mixture of the sulphates of the antibiotic substances produced by *Micromonospora purpurea*. It has a potency not less than 590 µg of gentamicin per mg, calculated with reference to the anhydrous substance.

Identification : (A) Dissolve 10 mg in 1 ml of *water* and add 5 ml of a 40 per cent w/v solution of *sulphuric acid*. Heat in a water-bath for 100 minutes. Cool and add sufficient *water* to produce 25 ml. The light absorption of a 1-cm layer of the resulting solution shows no maximum in the range of 220 to 300 nm, Appendix 5.15 A.

(B) Carry out the method for *paper chromatography (descending)*, Appendix 5.4.2. Prepare a chromatogram, using a slow-running paper like Whatman No. 20. Shake together 10 volumes of *chloroform*, 5 volumes of *methyl alcohol*, 3 volumes of *strong ammonia solution*, and 2 volumes of *water* and allow to separate. Use as the stationary phase the upper layer contained in a vessel placed on the bottom of the tank and surrounded by a portion of the lower layer. Use the remainder of the lower layer as the mobile phase.

Apply separately to the paper 2 µl of each of two solutions containing (1) 5 per cent w/v of the substance being examined and (2) 5 per cent w/v of *gentamicin R.S.* Elute for five hours, dry the paper at 105° for one hour, spray with a 0.25 per cent w/v solution of *ninhydrin* in a mixture of equal volumes of *pyridine* and *acetone*, and heat at 105° for two minutes. The three principal spots in the chromatogram obtained with solution (1) correspond to the three principal spots in the chromatogram obtained with solution (2).

(C) A solution (1 in 20) gives the reactions of *sulphates*, Appendix 3.1.

Specific optical rotation : Between +107° and +121°, determined in a 10.0 per cent w/v solution in *water*, Appendix 5.12.

pH : Between 3.5 and 5.5, determined in a 4.0 per cent w/v solution, Appendix 5.10

Sulphated ash : Not more than 1.0 per cent, Appendix 3.2.7.

Water : Not more than 15.0 per cent w/w, Appendix 3.3.25.

Assay : Carry out the *microbiological assay of antibiotics, Method A*, Appendix 4.1, and express the result in µg of gentamicin per mg.

Gentamicin Sulphate intended for parenteral administration complies with the following additional requirements:

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using 1 ml per kg of the rabbit's weight of a solution containing the equivalent of 10 mg of gentamicin per ml.

Sterility : Complies with the *tests for sterility*, Appendix 4.6.

Undue toxicity : Complies with the test described under Bacitracin, the dose being 0.5 ml of a solution containing the equivalent of 1 mg of gentamicin per ml in *water for injection*.

Storage : Store in well-closed containers and in a cool place.

Labelling : The label on the container states (1) the content of gentamicin in µg per mg; (2) the date after which the contents are not intended to be used; (3) the storage conditions; (4) whether or not the contents are intended for parenteral administration.

Gentamicin Injection

Category : Antibacterial.

Dose : By intramuscular injection, the equivalent of 80 to 240 mg of gentamicin daily, in divided doses.

By intravenous injection, the equivalent of 1 mg of gentamicin per kg in 100 to 200 ml of Sodium Chloride Injection or 5 per cent Dextrose Injection.

Usual strength : 80 mg in 2 ml.

Description : Clear, colourless to pale-yellow solution with a faint odour

Standards : Gentamicin Injection is a sterile solution of Gentamicin Sulphate in Water for Injection containing suitable stabilising agents. It contains not

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

less than 95.0 per cent and not more than 110.0 per cent w/v of the stated amount of gentamicin.

Identification : (A) To a volume equivalent to 40 mg of gentamicin, add 5 ml of *water* and shake with three quantities, each of 5 ml, of *chloroform*. Filter the aqueous layer and to 1 ml of the filtrate add 5 ml of a 40 per cent w/v solution of *sulphuric acid*. Heat in a water-bath for 100 minutes, cool, and add sufficient *water* to produce 25 ml. The light absorption of the resulting solution shows no maximum in the range 220 to 300 nm, Appendix 5.15 A.

(B) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using a silica gel 60 precoated plate and as the mobile phase the lower layer obtained by shaking together 1 volume of *chloroform*, 1 volume of *methyl alcohol* and 1 volume of *strong ammonia solution*, and allowing to separate. Apply separately to the plate (1) a volume of the injection equivalent to 30µg of gentamicin and (2) 0.1 mg of *gentamicin sulphate R.S.* dissolved in a volume of *water* equivalent to the volume of the injection used. After removal of the plate, allow it to dry in air, spray with a 0.25 per cent w/v solution of *ninhydrin* in a mixture of equal volumes of *pyridine* and *acetone* and heat at 105° for two minutes. The three principal spots in the chromatogram obtained with solution (1) correspond to the three principal spots in the chromatogram obtained with solution (2).

pH : Between 3.0 and 5.0, Appendix 5.10.

Other requirements : Complies with the requirements stated under Injections.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using a volume equivalent to not less than 10 mg of gentamicin, diluted to not more than 5 ml with *water for injection* per kg of the rabbit's weight.

Undue toxicity : Complies with the test for **Undue toxicity**, described under Gentamicin Sulphate, using a volume equivalent to 0.5 mg of gentamicin diluted to 0.5 ml with *water for injection*.

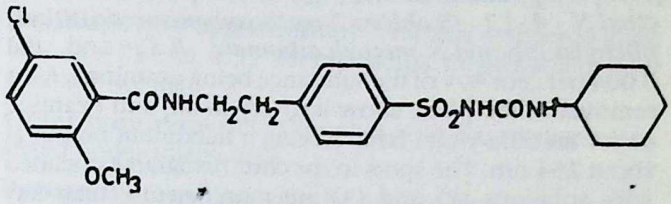
Assay : Carry out the *microbiological assay of antibiotics, Method A*, Appendix 4.1, and express the result in mg of gentamicin in 2 ml.

Storage : Store in single-dose or multiple-dose containers.

Labelling : The label on the container states the strength in mg of gentamicin in 2 ml.

Glibenclamide

Glybenclamide



$C_{23}H_{28}ClN_3O_5S$ Mol. Wt. 494.00

Category : Antidiabetic (oral).

Dose : 2.5 to 20 mg once daily, after food.

Description : White or almost white, crystalline powder; odourless or almost odourless.

Solubility : Practically insoluble in *water*, and in *solvent ether*; slightly soluble in *alcohol*; sparingly soluble in *chloroform*.

Standards : Glibenclamide is 1-[4-{2-(5-chloro-2-methoxybenzamido)ethyl}benzenesulphonyl]3-cyclohexylurea. It contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of $C_{23}H_{28}ClN_3O_5S$, calculated with reference to the dried substance.

Identification : (A) Boil 50 mg with 1 ml of *6N sodium hydroxide*; the fumes evolved as soon as the water is evaporated; change moistened *red litmus paper* to blue and have a pungent, amine-like odour.

(B) Mix 0.2 g with 0.25 g of *anhydrous sodium carbonate* and 0.25 g of *potassium carbonate*. Ignite for ten minutes, cool, add to the residue 10 ml of hot *water*, stir for one minute, and filter. The filtrate gives the reactions of *chlorides*, and of *sulphates*, Appendix 3.1.

(C) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.01 per cent w/v solution in *0.01N methanolic hydrochloric acid* exhibits a maximum at 300 nm and a less intense maximum at 275 nm; *extinction* at 300 nm, about 0.63, Appendix 5.15 A.

Melting range : Between 172° and 174°, Appendix 5.11.

Clarity and colour of solution : A 1.0 per cent w/v solution in *alcohol* is clear and colourless.

Heavy metals : Not more than 20 parts per million, determined on 1 g by Method B, Appendix 3.2.4.

Foreign substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel GF 254* as the coating substance and a mixture of 45 volumes of *chloroform*, 45 volumes of *cyclohexane*, 5 volumes of *alcohol* and 5 volumes of *glacial acetic acid* as the mobile phase. Apply separately to the plate 10µl of each of four solutions in a mixture of equal volumes of

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

methyl alcohol and *chloroform* containing (1) 2.0 per cent w/v of the substance being examined, (2) 0.008 per cent w/v of *4-[2-(5-chloro-2-methoxybenzamido) ethyl] phenylsulphonamide R.S.*, (3) 0.008 per cent w/v of *ethyl N - 4 - [2 - (5-chloro-2-methoxybenzamido) ethyl] phenylsulphonyl-N-methylcarbamate R.S.*, and (4) 0.004 per cent w/v of the substance being examined. After removal of the plate, allow it to dry in air, and examine under an ultra-violet lamp having a maximum output at about 254 nm. The spots in the chromatograms obtained with solutions (2) and (3) are more intense than any corresponding spots in the chromatogram obtained with solution (1). Any additional spot in the chromatogram obtained with solution (1), other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (4).

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 100° to 105°, Appendix 5.8.

Sulphated ash : Not more than 0.2 per cent, Appendix 3.2.7.

Assay : Weigh accurately about 0.5 g and dissolve in 100 ml of hot *alcohol*, previously neutralised to *phenolphthalein solution*. Titrate with *0.1N sodium hydroxide*, using *phenolphthalein solution* as indicator, taking care to avoid exposure to atmospheric carbon dioxide. Each ml of *0.1N sodium hydroxide* is equivalent to 0.0494 g of $C_{23}H_{28}ClN_3O_5S$.

Storage : Store in well-closed, light-resistant containers.

Glibenclamide Tablets

Category : Antidiabetic.

Dose : Glibenclamide, 2.5 to 20 mg once daily, after food.

Usual strength : 5 mg.

Standards : Glibenclamide Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Glibenclamide, $C_{23}H_{28}ClN_3O_5S$.

Identification : The light absorption, in the range 230 to 350 nm, of the solution obtained in the **Assay** exhibits a maximum at 300 nm and a less intense maximum at 275 nm, Appendix 5.15 A.

Uniformity of content : Powder one table, warm with 10 ml of *0.1N methanolic hydrochloric acid* and centrifuge. Repeat the extraction with three further quantities, each of 10 ml, of *0.1N methanolic hydrochloric acid*. Cool the combined extracts and add sufficient *0.1N methanolic hydrochloric acid* to produce 50 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 300 nm, Appendix 5.15 A. Calculate the content of $C_{23}H_{28}ClN_3O_5S$, taking 63 as the value of E(1 per cent, 1-cm) at the maximum at about 300 nm.

Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 90 per cent and 110 per cent of the average except that for one tablet the content may be between 85 per cent and 115 per cent of the average.

Foreign substances : Carry out the test for **Foreign substances** described under Glibenclamide, applying to the plate 20 µl of each of the following four solutions: For solution (1) extract a quanity of the powdered tablets equivalent to 20 mg of Glibenclamide with four quantities, each of 5 ml, of a mixture of two volumes of *methylene chloride* and one volume of *acetone*; evaporate the combined extracts to dryness in "in vacuo" at a temperature not exceeding 40° and dissolve the residue in 4 ml of a mixture of equal volumes of *chloroform* and *methyl alcohol*. Solution (2) is a 0.012 per cent w/v solution of *4-[2-(5-chloro-2-methoxybenzamido) ethyl]-phenylsulphonamide R.S.* in a mixture of equal volumes of *chloroform* and *methyl alcohol*. Solution (3) is a 0.002 per cent w/v solution of *ethyl N-4-[2-(5-chloro-2-methoxybenzamido) ethyl] phenylsulphonyl-N-methylcarbamate R.S.* in a mixture of equal volumes of *chloroform* and *methyl alcohol*. Solution (4) is a 0.5 per cent w/v solution of *glibenclamide R.S.* in a mixture of equal volumes of *chloroform* and *methyl alcohol*. The spots in the chromatograms obtained with solutions (2) and (3) are more intense than any corresponding spots in the chromatogram obtained with solution (1)

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 20 mg of Glibenclamide and shake with 40 ml of *0.1N methanolic hydrochloric acid*. Heat gently and centrifuge. Repeat the extraction with three further quantities, each of 20 ml of *0.1N methanolic hydrochloric acid*. To the combined extracts add sufficient *0.1N methanolic hydrochloric acid* to produce 200 ml and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 300 nm, Appendix 5.15 A. Calculate the content of $C_{23}H_{28}ClN_3O_5S$, taking 63 as the volume of E(1 per cent, 1-cm) at the maximum at about 300 nm.

Human Normal Immunoglobulin

Immune Human Serum Globulin; Human Gamma Globulin

Category : Passive immunising agent.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Dose : By intramuscular injection, a volume equivalent to the following amount of protein:

For the prevention of measles, from 250 mg, for infants under one year, to 750 mg for children of three years and over; for the attenuation of measles, 250 mg.

For the prevention of rubella in pregnant women, 750 mg.

For the prevention of infective hepatitis, 250 mg upto ten years of age, 750 mg over ten years.

Description : Transparent or slightly opalescent liquid, colourless or brownish in colour which on storage may show a slight granular deposit; almost odourless.

Standards : Human Normal Immunoglobulin is a sterile solution containing antibodies derived from human blood. It contains almost all the gamma-G globulins, together with smaller amounts of other plasma proteins obtained from source materials such as the blood, plasma or serum of blood donors who have been shown by appropriate clinical and laboratory tests to be healthy. No antibiotic is added to the source materials used for the preparation of immunoglobulin.

It is prepared from pooled material of a minimum volume of 25 litres by a method which has been shown: (a) to be capable of concentrating tenfold from source material at least two different antibodies, one viral and one bacterial, for which an international standard or reference preparation is available, (b) not to affect the integrity of the globulins, (c) to consistently yield a product which is safe for intramuscular injection, and (d) not to transmit viral hepatitis or any other infection.

Low temperatures or aseptic techniques are used to minimise contamination by micro-organisms. The separated globulins are dissolved in a vehicle containing suitable preservative or stabilising agent. The final solution is sterilised by Filtration and distributed in previously sterilised containers which are then sealed so as to exclude micro-organisms.

It contains not less than 10.0 and not more than 18.0 per cent w/v of protein.

Identification : (A) By precipitation with specific antisera the solution is shown to contain proteins of human origin only.

(B) Examine by *electrophoresis*, using the moving boundary technique and a 1.0 per cent w/v solution in *barbitone buffer solution pH 8.6* and of ionic strength 0.1. At least 90 per cent w/v of the protein has a mobility not greater than $-2.8 \times 10^{-5} cm^2 V^{-1} S^{-1}$, Appendix 5.9.

pH : Between 6.4 and 7.2, Appendix 5.10.

Stability : Heat approximately 2 ml in a stoppered glass tube 12 × 75 mm, at 57° for four hours; no gelation or flocculation occurs.

Other requirements : Complies with the requirements stated under Injections.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36 using not less than 1 ml per kg of the rabbit's weight.

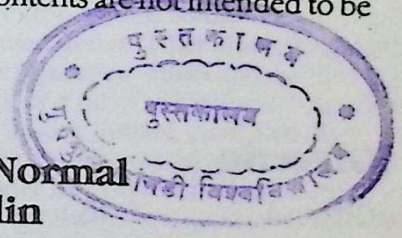
Sterility : Complies with the *tests for sterility*, Appendix 4.6.

Undue toxicity : Complies with the *test for undue toxicity for vaccines and sera*, Appendix 2.37, using 0.5 ml of the solution for each mouse and 5 ml for each guinea-pig.

Assay : Dilute a suitable volume with *water* to produce a solution containing 1 per cent w/v of protein and carry out the **Assay** described under Normal Human Plasma using 1.5 ml of the dilution in a round-bottomed centrifuge tube.

Storage : Store in colourless glass containers, protected from light, at a temperature between 2° and 10°.

Labelling : The label on the container states (1) the volume and the protein concentration; (2) the recommended human dose; (3) the name and quantity of any preservative or stabilising agent; (4) "for intramuscular injection only"; (5) the type of source material; (6) the storage conditions; (7) the date after which the contents are not intended to be used.



Dried Human Normal Immunoglobulin

Dried Human Gamma Globulin

Category : Passive immunising agent.

Dose : By intramuscular injection, a volume of reconstituted solution equivalent to the following amount of protein:

For the prevention of measles, from 250 mg, for infants under one year, to 750 mg for children of three years and over; for the attenuation of measles, 250 mg.

For the prevention of rubella in pregnant women, 750 mg.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

For the prevention of infective hepatitis, 250 mg upto ten years of age, 750 mg over ten years.

Description : White or slightly yellowish powder or a solid, friable mass, completely soluble in *water for injection.*

Standards : Dried Human Normal Immunoglobulin is prepared from a pool of Human Normal Immunoglobulin by freeze-drying. The final immunoglobulin solution is distributed into its final sterile containers, dried, and the containers are sealed so as to exclude air, moisture and microbial contamination.

Water : Not more than 1.0 per cent w/w, Appendix 3.3.25.

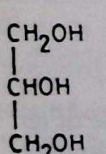
Reconstitute the contents of the sealed container with the requisite amount of *sterile water for injection.* The reconstituted solution complies with the tests for **Identification, pH, Pyrogen, Sterility, Undue toxicity** and **Assay,** described under Human Normal Immunoglobulin.

Storage : Store in a cool place, protected from light.

Labelling : The label on the container states (1) the weight of protein; (2) the recommended human dose; (3) the name and quantity of the reconstituting liquid to be added; (4) that the material should be used immediately after it has been reconstituted; (5) the name and quantity of any preservative or stabilising agent; (6) "for intramuscular injection only"; (7) the type of source material; (8) the storage conditions; (9) the date after which the contents are not intended to be used.

Glycerin

Glycerol



$C_3H_8O_3$ Mol. Wt. 92.09

Category : Pharmaceutical aid (humectant; soluent).

Description : Clear, colourless liquid of syrupy consistency; odourless; taste, sweet followed by a sensation of warmth. It is hygroscopic.

Solubility : Miscible with *water* and with *alcohol*; practically insoluble in *chloroform*, in *solvent ether* and in fixed oils.

Standards : Glycerin is 1,2,3-propanetriol. It contains not less than 98.0 per cent w/w of $C_3H_8O_3$.

Identification : (A) Heat a few drops with 0.5 g of *potassium bisulphate*; acrolein is evolved which is recognised by its characteristic pungent odour.

(B) Heat in a Bunsen flame on a borax bead; it produces a green flame.

(C) Mix 1 ml with ten drops of *nitric acid.* Superpose ten drops of *potassium dichromate solution.* A blue ring is formed at the interface of the liquids. The blue colour does not diffuse into the lower layer in ten minutes.

Acidity : To 50 ml of a 50 per cent w/v solution add 0.2 ml of *dilute phenolphthalein solution*; not more than 0.2 ml of *0.1 N sodium hydroxide* is required to produce a pink colour.

Wt. per ml : Between 1.252 g and 1.257 g, Appendix 5.19, corresponding to between 98.0 per cent and 100.0 per cent w/w of $C_3H_8O_3$.

Refractive index : Between 1.470 and 1.475 determined at 20°, Appendix 5.14.

Arsenic : Not more than 2 parts per million, Appendix 3.2.1.

Copper : To 10 ml add 30 ml of *water*, mix, add 1 ml of *dilute hydrochloric acid*, add 10 ml of *hydrogen sulphide solution*; no colour is produced.

Iron : 10 g complies with the *limit test for iron*, Appendix 3.2.5.

Heavy metals : Not more than 5 parts per million, determined by Method A on a solution of 4 g in 2 ml of *0.1 N hydrochloric acid* and sufficient *water* to produce 25 ml, Appendix 3.2.4.

Sulphate : 1 ml complies with the *limit test for sulphates*, Appendix 3.2.8.

Chloride : 1 ml complies with the *limit test for chlorides*, Appendix 3.2.2.

Acraldehyde and glucose : Heat strongly; it assumes not more than a faint yellow, and not a pink colour. Heat further; it burns with little or no charring and with no odour of burnt sugar.

Aldehydes and related substances : To 12.5 ml of a 50 per cent w/v solution in a glass-stoppered flask add 2.5 ml of *water* and 1 ml of *decolorised magenta solution*, close the flask and allow to stand for one hour. Any violet colour produced is not more intense than that produced by mixing 1.6 ml of *0.1 N potassium permanganate* and 250 ml of *water.*

Sugar : Heat 5 g with 1 ml of *dilute sulphuric acid* for five minutes on a water-bath. Add 2 ml of *dilute sodium hydroxide solution* and 1 ml of *copper sulphate solu-*

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

tion. A clear, blue coloured solution is produced. Continue heating on the water-bath for five minutes. The solution remains blue and no precipitate is formed.

Fatty acids and esters : Mix 50 g with 50 ml of freshly boiled *water* and 50.0 ml of *0.5N sodium hydroxide*, boil the mixture for five minutes, cool, add a few drops of *phenolphthalein solution* and titrate the excess alkali with *0.5N hydrochloric acid*. Perform a blank determination. Not more than 1 ml of *0.5N sodium hydroxide* is consumed.

Sulphated ash : Not more than 0.01 per cent, Appendix 3.2.7.

Storage : Store in tightly-closed containers.

Glyceryl Monostearate

Monostearin

Category : Pharmaceutical aid (emulsifying agent; for external use only).

Description : White or almost white, hard, waxy mass, powder or flakes; almost odourless; taste, faint and fatty.

Solubility : Freely soluble in *chloroform*; soluble in *solvent ether*, in *benzene*, and in *alcohol* at 60°; practically insoluble in *water*.

Standards : Glyceryl Monostearate is a mixture of monoglycerides of stearic and palmitic acids, together with variable quantities of di- and tri-glycerides. It contains not less than 35.0 per cent of monoglycerides, calculated as $C_{20}H_{40}O_4$, and not more than 7.0 per cent of free glycerol.

Identification : (A) Heat 1 g with 2 g of *potassium bisulphate* in an evaporating dish. Instant fumes are evolved which darken filter paper impregnated with *alkaline potassium mercuri-iodide solution*.

(B) Heat 2.5 g with 40 ml of *alcoholic potassium hydroxide solution* for 30 minutes on a water-bath under a reflux condenser. Add 30 ml of *water*, evaporate the alcohol, acidify the hot mixture with 15 ml of *dilute hydrochloric acid*, cool and extract with 50 ml of *solvent ether*. Wash the ether layer with two quantities, each of 10 ml, of 20 per cent w/v solution of *sodium chloride*, dry the ether extract over *anhydrous sodium sulphate* and filter. Evaporate the solvent and dry the residue "in vacuo". Melt the residue and fill one or two capillary tubes (for the determination of melting range) and allow to stand for 24 hours in a desiccator. Carry out the *determination of melting range* by Method II, Appendix 5.11. The residue melts between 53° and 57°.

Melting range : Between 54° and 60°, determined by Method II, Appendix 5.11.

Acid value : Not more than 5.0, determined on 0.5 g dissolved in 50 ml of a mixture of equal volumes of *alcohol* and *solvent ether*, Appendix 3.3.15.

Iodine value : Not more than 5.0, Appendix 3.3.18.

Saponification value : Between 155 and 170, Appendix 3.3.20.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Water : Not more than 2.0 per cent, determined on 0.5 g dissolved in a mixture of 10 ml of *dehydrated methyl alcohol* and 10 ml of *chloroform*, Appendix 3.3.25.

Assay : Weigh accurately about 0.4 g and dissolve in 50 ml of *chloroform* in a glass stoppered separating funnel. Add 25 ml of *water* and shake vigorously for one minute. Allow the layers to separate (if an emulsion is formed, add a few drops of *glacial acetic acid*). Repeat the extraction with three further quantities, each of 25, 20 and 20 ml of *water*. Filter the aqueous layers through a filter paper moistened with *water*, wash the filter with two quantities, each of 5 ml, of *water* and dilute the combined filtrate and washings to 100.0 ml with *water*.

Free glycerol : To 50.0 ml of the aqueous solution in a 400-ml conical flask fitted with a ground-glass stopper, add 25.0 ml of *periodic-acetic acid solution*, shaking cautiously. Allow to stand for 30 minutes at a temperature between 25° and 30°. Add 100 ml of *water* and 12 ml of *potassium iodide solution*. Titrate the liberated iodine with *0.1N sodium thiosulphate*, using *starch solution* as indicator. Carry out a blank Assay under the same conditions using 50 ml of *water* instead of the 50 ml of the solution to be examined. 1 ml of *0.1N sodium thiosulphate* is equivalent to 0.0023 g of glycerol.

Monoglycerides : Carry out the **Assay** on the chloroform solution obtained above. Filter through a cotton wool plug. Wash the separating funnel and the filter with three quantities, each of 5 ml of *chloroform*. Pour the filtrate and washings into a 100-ml graduated flask and dilute to volume with *chloroform*. Mix and carry out the **Assay** described under free Glycerol using 50 ml of the chloroform solution. 1 ml of *0.1N sodium thiosulphate* is equivalent to 0.0172 g of monoglycerides, calculated as glycerol monostearopalmitate ($C_{20}H_{40}O_4$).

The quantity of *0.1N sodium thiosulphate* used in the Assay is not less than 85 per cent of the quantity of thiosulphate used in the blank Assay.

Storage : Store in well-closed, light-resistant containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Glyceryl Trinitrate Tablets

Nitroglycerin Tablets

Category : Vasodilator (coronary).

Dose : Glyceryl Trinitrate, 0.5 to 1 mg.

Usual strengths : 0.2 mg; 0.3 mg; 0.5 mg; 0.6 mg.

Standards : Glyceryl Trinitrate Tablets contain not less than 80.0 per cent and not more than 120.0 per cent of the stated amount of Glyceryl Trinitrate, $C_3H_5N_3O_9$.

Disintegration : The requirement for disintegration does not apply to Glyceryl Trinitrate Tablets.

Other requirements : Comply with the requirements stated under Tablets.

Uniformity of content : Place one tablet in a centrifuge tube containing a few glass beads, add 5.0 ml of a 90 per cent v/v solution of *glacial acetic acid*, shake for one hour and centrifuge.

For tablets containing the equivalent of 0.4 to 0.6 mg of Glyceryl Trinitrate carry out the **Assay** on 2.0 ml of the resulting solution, beginning at the words "add 2 ml of *phenoldisulphonic acid solution* ....".

For tablets containing 0.2 to 0.3 mg of Glyceryl Trinitrate carry out the test in the manner described but measure the *extinction* of 2-cm layers of the solutions.

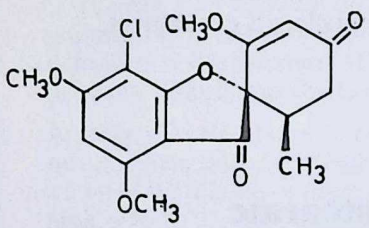
Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 80 and 120 per cent of the average except that for one tablet the content may be between 75 and 125 per cent of the average.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 0.5 mg of Glyceryl Trinitrate, add 5.0 ml of a 90 per cent v/v solution of *glacial acetic acid*, shake for one hour and centrifuge. To 2.0 ml of the supernatant liquid add 2 ml of *phenoldisulphonic acid solution* and allow to stand for fifteen minutes. Add 8 ml of *water*, made alkaline with *strong ammonia solution*, cool to about 20°, dilute to 20.0 ml with *water*, and filter. Measure the *extinction* of a 1-cm layer of the filtrate at 405 nm, Appendix 5.15 A, using as the blank 2.0 ml of a 90 per cent v/v solution of *glacial acetic acid*, treated in a similar manner, beginning at the "add 2 ml of *phenoldisulphonic acid solution*.....". Dissolve 133.5 mg of *potassium nitrate*, previously dried at 105°, in sufficient *water* to produce 100.0 ml; to 10.0 ml add sufficient *glacial acetic acid* to produce 100.0 ml. Using 2.0 ml of this solution, repeat the Assay beginning at the words "add 2 ml of *phenoldisulphonic acid solution*". Calculate the content of $C_3H_5N_3O_9$ from the values of the *extinctions* so obtained. Each ml of the potassium nitrate solution is equivalent to 0.1 mg of $C_3H_5N_3O_9$.

Storage : Store in well-closed, light-resistant containers in a cool dry place.

Labelling : The label on the container states (1) that the tablets should be allowed to dissolve slowly in the mouth; (2) the date after which the tablets are not intended to be used; (3) the storage conditions

Griseofulvin



$C_{17}H_{17}ClO_6$ Mol. Wt. 352.77

Category : Antifungal.

Dose : 0.5 to 1 g daily, in divided doses.

Description : White to pale cream powder, the particles of which are generally upto 5 μm in maximum dimension with only a few larger particles exceeding 30 μm; almost odourless; tasteless.

Solubility : Very slightly soluble in *water*; soluble in *chloroform*; slightly soluble in *ethyl alcohol*, and in *methanol*.

Standards : Griseofulvin is (2*S*, 6′*R*)-7 chloro-2′, 4, 6-trimethoxy-6′-methylbenzofuran-2-spiro-1′-cyclohex-2′-ene-3,4′-dione. It contains not less than 97.0 per cent and not more than the equivalent of 102.0 per cent of $C_{17}H_{17}ClO_6$, calculated with reference to the dried substance.

Identification : Dissolve about 5 mg in 1 ml of *sulphuric acid* and add 5 mg of powdered *potassium dichromate*. A wine-red colour is produced.

Melting range : Between 218° and 224°, Appendix 5.11.

Specific surface area : Between 1.3 and 1.7 square meters per g, Appendix 5.17.

Specific optical rotation : Between +354° and +364°, determined at 20° in a 1.0 per cent w/v solution in *dimethylformamide*, Appendix 5.12.

Clarity and colour of solution : A 7.5 per cent w/v solution in *dimethylformamide* is clear and not more intensely coloured than a mixture of 1.2 ml of *ferric chloride C.S.*; 0.3 ml of *cobalt chloride C.S.* and 98.5 ml of *hydrochloric acid (1 per cent w/v)*.

Acidity : Suspend 0.25 g in 20 ml of *alcohol* and titrate

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

with *0.2N sodium hydroxide*, using *phenolphthalein solution* as indicator. Not more than 1.0 ml is required.

Heavy metals : Not more than 20 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

Undue toxicity : 1.0 ml of a suspension of 0.1 g in *water* given by mouth to each of five healthy mice, each weighing between 17 and 22 g, does not cause death of any of the mice within 48 hours. If one or more animals die within 48 hours, repeat the test one or more times using for each test five or more previously unused mice. The sample passes the test if the total number of deaths is not greater than 10 per cent of the total number of animals tested, including the original test

Sulphated ash : Not more than 0.2 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 80 mg and dissolve in sufficient *ethyl alcohol* to produce 200.0 ml. Dilute 2.0 ml to 100.0 ml with *ethyl alcohol* and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 291 nm, Appendix 5.15 A. Calculate the content of $C_{17}H_{17}ClO_6$, taking 686 as the value of E(1 per cent, 1-cm) at the maximum at about 291 nm.

Storage : Store in well-closed containers.

Labelling : The label on the container states (1) the date after which the contents are not intended to be used; (2) the storage conditions.

Griseofulvin Tablets

Category : Antibiotic (antifungal).

Dose : Griseofulvin, 0.5 to 1 g daily, in divided doses.

Usual strength : 125 mg.

Standards : Griseofulvin Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Griseofulvin, $C_{17}H_{17}ClO_6$.

Identification : Dissolve about 5 mg of the powdered tablets in 1 ml of *sulphuric acid* and add 5 mg of powdered *potassium dichromate*; a wine-red colour is produced.

Particle size : Shake one tablet thoroughly with about 2 ml of *water*; mix one drop of the resulting suspension with 2 ml of *water* containing one drop of *polysorbate 80*. Mount one drop of the mixture on a slide and examine under a microscope; the particles of Griseofulvin are generally up to 5 µm in maximum dimension with only a few larger particles exceeding 30 µm.

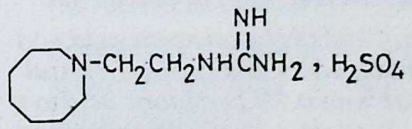
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 80 mg of Griseofulvin and boil with 150 ml of *ethyl alcohol* for fifteen minutes under a reflux condenser and cool. Add sufficient *ethyl alcohol* to produce 200.0 ml, shake and centrifuge. Dilute 2.0 ml of the supernatant liquid to 100 ml with *ethyl alcohol* and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 291 nm, Appendix 5.15 A. Calculate the content of $C_{17}H_{17}ClO_6$, taking 686 as the value of E(1 per cent, 1-cm) at the maximum at about 291 nm.

Storage : Store in well-closed containers.

Labelling : The label on the container states (1) the date after which the tablets are not intended to be used; (2) the storage conditions.

Guanethidine Sulphate



$C_{10}H_{22}N_4, H_2SO_4$ Mol.Wt. 296.39

Category : Antihypertensive.

Dose : Initial dose, 10 to 20 mg daily; subsequent doses, increasing at weekly intervals to a maximum of 300 mg daily, in accordance with the needs of the patient.

Description : White or almost white, crystalline powder; almost odourless.

Solubility : Freely soluble in *water*; slightly soluble in *alcohol*; practically insoluble in *chloroform* and in *solvent ether*.

Standards : Guanethidine Sulphate is 1-[2-(perhydroazocin-1-yl) ethyl] guanidine sulphate (1:1). It contains not less than 98 per cent and not more than the equivalent of 102.0 per cent of $C_{10}H_{22}N_4, H_2SO_4$, calculated with reference to the dried substance.

Identification : (A) Dissolve 25 mg in 5 ml of *water*, add 1.5 ml *sodium hydroxide solution*, 1 ml of *α-naphthol solution*, add, dropwise with shaking 0.5 ml of *chlorinated soda solution*; a bright pink precipitate is produced which becomes red on standing.

(B) Weigh about 25 mg and dissolve in 25 ml of *water*, and add 20 ml of *picric acid solution*; the precipitate; after washing with water melts at about 153°, Appendix 5.11.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

(C) A solution (1 in 20) gives the reaction of *sulphates*, Appendix 3.1.

Clarity and colour of solution : A 2.0 per cent w/v solution is clear and colourless.

pH : Between 5.0 and 6.0, determined in a 2.0 per cent w/v solution, Appendix 5.10.

Heavy metals : Not more than 10 parts per million, determined on 2.0 g by Method B, Appendix 3.2.4.

Oxidisable substances : Dissolve 1.0 g in 25 ml of *water* and add 25 ml of *2N sodium hydroxide*. Allow to stand for ten minutes, add 1 g of *potassium bromide* and 1 ml of *0.05N potassium bromate* and acidify with 30 ml of *2N hydrochloric acid*. Mix and allow to stand for five minutes, protected from light. Add 2 g of *potassium iodide*, shake, allow to stand for two minutes and titrate with *0.05N sodium thiosulphate* using *starch solution* as indicator. Not less than 0.3 ml of *0.05N sodium thiosulphate* is required.

Sulphated ash : Not more than 0.2 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Dissolve 0.4 g in 40 ml of *glacial acetic acid*, add 20 ml of *acetic anhydride*, add a few drops of *crystal-violet solution* and titrate with *0.1N perchloric acid* to a bluish-green end-point. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02964 g of $C_{10}H_{22}N_4, H_2SO_4$.

Storage : Store in well-closed containers in a cool place.

Guanethidine Tablets

Category : Antihypertensive.

Dose : Guanethidine Sulphate. Initial dose, 10 to 20 mg daily; subsequent doses, increasing at weekly intervals to a maximum of 300 mg daily, in accordance with the needs of the patient.

Usual strengths : 10 mg; 25 mg.

Standards : Guanethidine Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Guanethidine Sulphate, $C_{10}H_{22}N_4, H_2SO_4$.

Identification : Extract a quantity of the powdered tablets equivalent to about 50 mg of Guanethidine Sulphate with a mixture of 5 ml of *hydrochloric acid* and 45 ml of *water*, filter; neutralise 25 ml of the filtrate with *sodium hydroxide solution*, and add 20 ml of *picric acid solution*; the precipitate, after washing with *water* melts at about 153°, Appendix 5.11.

Uniformity of content (for 10 mg tablets only) : Crush one tablet, add 15 ml of *water* and shake for fifteen minutes. Add sufficient *water* to produce 25.0 ml and centrifuge. On 5.0 ml of the clear, supernatant liquid complete the **Assay** beginning at the words "add 10.0 ml of a solution . . . . .". Calculate the content of $C_{10}H_{22}N_4, H_2SO_4$.

Repeat the operation with a further nine tablets and calculate the average content of the ten tablets: The content of each tablet is between 85 per cent and 125 per cent of the average except that for one tablet the content may be between 80 per cent and 120 per cent of the average.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 30 mg of Guanethidine Sulphate, shake for fifteen minutes with 50 ml of *water*, dilute to 100.0 ml with *water*, and filter. To 5.0 ml of the filtrate add 10.0 ml of a solution prepared by dissolving 1 g of *sodium nitroprusside* and 1 g of *potassium ferrocyanide* in 50 ml of a 0.5 per cent w/v solution of *sodium hydroxide*, adding 5 ml of *strong hydrogen peroxide solution*, swirling gently, and diluting to 100.0 ml with the sodium hydroxide solution. Mix, allow to stand for twenty minutes, add sufficient *water* to produce 25.0 ml, and measure the *extinction* of the resulting soultion at 520 nm, Appendix 5.15 A, using as the blank a solution prepared by treating 5 ml of *water* in a similar manner, beginning at the words "add 10 ml of a solution . . . . .". Calculate the content of $C_{10}H_{22}N_4, H_2SO_4$ from the *extinction* obtained by repeating the operation using 5 ml of 0.03 per cent w/v solution of *guanethidine sulphate R.S.*, beginning at the words "add 10.0 ml of a solution", and from the declared content of $C_{10}H_{22}N_4, H_2SO_4$ on the *guanethidine sulphate R.S.*

Storage : Store in light-resistant containers.

Guar Gum

Category : Pharmaceutical aid (tablet binder; tablet disintegrant).

Description : Almost white to pale yellowish-white powder; taste and odour, characteristic. When examined in lactophenol mount, under a microscope it shows irregular, angular particles of various sizes and shape and when examined in water mount, it rapidly swells forming a translucent suspension.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Solubility : When stirred with 50 parts of *water*, a thick jelly is formed which with further addition of 150 parts of *water*, yields a thick transparent suspension; practically insoluble in *alcohol*.

Standards : Guar Gum is a gum obtained from the ground endosperms of the seeds of *Cyamopsis tetragonolobus* (Linn.) Taub or other species of *Cyamopsis* (Fam. Leguminosae). It consists mainly of a high molecular weight hydro-colloidal polysaccharide, composed of galactan and mannan units combined through glycosidic linkages.

Identification : (A) To 0.1 g add 1 ml of *0.2N iodine*, the mixture does not acquire an olive-green colour.

(B) Dissolve 0.1 g in 20 ml of *water* by shaking and add 0.5 ml of *hydrogen peroxide solution* and 0.5 ml of a 1 per cent w/v solution of *benzidine* in *alcohol (90 per cent)*, shake and allow to stand; no blue colour is produced (distinction from acacia).

(C) Mount a small quantity in *ruthenium red solution* and examine microscopically; the particles do not acquire a pink colour (distinction from sterculia gum and agar).

(D) To a 0.5 per cent w/v solution, add a 20 per cent w/v solution of *lead acetate*; a flocculent precipitate is produced (distinction from acacia, ghatti gum and sterculia).

Acidity or Alkalinity : A 0.5 per cent w/v solution is neutral to *litmus*.

Tannin : To 5 ml of a 0.5 per cent w/v solution, add 0.1 ml of *ferric chloride test-solution*; no bluish-black colour is produced.

Starch : Mount a small quantity on *0.02N iodine* and examine under a microscope; no bluish particles are visible.

Arsenic : Not more than 3 parts per million, Appendix 3.2.1.

Heavy metals : Not more than 20 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

Protein : Not more than 5.0 per cent determined in the following manner: Carry out the *determination of nitrogen*, Appendix 3.3.5, using about 3.5 g accurately weighed substance and multiply the percentage of nitrogen determined by 6.25 to obtain the percentage of protein.

Acid-insoluble matter : Not more than 3.0 per cent, determined in the following manner: Weigh accurately about 1.5 g and disperse in 150 ml of *water* and 1.5 ml of *sulphuric acid*. Warm on a water-bath for six hours, replacing any water lost by evaporation. Add about 0.5 g of a suitable filter-aid, accurately weighed, and filter through a suitable ashless filter. Wash the residue several times with hot *water*, dry the filter and its contents at 105° for three hours. Cool in a desiccator, weigh and subtract the weight of the filter-aid.

Microbial limits : Total bacterial count does not exceed 5000 per g; 1 g meets the requirements of the test for the absence of *E. coli* and Salmonella, Appendix 4.5.

Ash : Not more than 2.0 per cent, Appendix 3.3.22.

Loss on drying : Not more than 13.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Storage : Store in tightly-closed containers.

Heparin Sodium

Category : Anticoagulant

Dose : For treatment, by intravenous injection, 20,000 to 50,000 Units daily.

For prophylaxis, by subcutaneous injection, 10,000 to 15,000 Units daily, in divided doses.

Description : White or greyish-white powder; odourless. Moderately hygroscopic.

Solubility : Soluble in *water*; soluble in *saline solution* forming a clear, colourless or straw-coloured liquid.

Standards : Heparin Sodium is a preparation containing the sodium salt of a complex organic acid present in mammalian tissues, and having the characteristic property of delaying the clotting of shed blood. It may be obtained from the lungs, intestinal mucosa, or other tissues of oxen, pigs or sheep. It contains not less than 110 Units per mg when derived from lungs and not less than 130 Units per mg when derived from other tissues, both calculated with reference to the dried substance.

Identification : (A) To 0.1 g, add 0.2 g of *sodium* and heat cautiously until the reaction with sodium is complete. Heat to bright red heat, and carefully plunge the tube and the contents into 5 ml of *water*. Filter, boil the filtrate for a few minutes with 20 mg of *ferrous sulphate*. Cool, acidify with *hydrochloric acid* and add one drop of *ferric chloride test-solution*; a blue colour is produced (distinction from dextran sulphate).

(B) A solution (1 in 20) gives the reaction of *sodium*, Appendix 3.1.

pH : Between 5.0 and 8.0, determined in a 1.0 per cent w/v solution, Appendix 5.10.

Light absorption : The *extinction* of a 1-cm layer of a 0.4 per cent w/v solution at 260 nm and 280 nm is not greater than 0.2 and 0.15 respectively, Appendix 5.15 A.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using 0.5 ml per kg of the rabbit's weight

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

of a solution in *water for injection* containing not less than 2000 Units per ml.

Protein : To 1 ml of a 1 per cent w/v solution, add 5 drops of a 20 per cent w/v solution of *trichloroacetic acid*; no precipitate or turbidity is produced.

Loss on drying : Not more than 8.0 per cent, determined on 1.0 g by drying "in vacuo at 60°", Appendix 5.8.

Assay : Carry out the *biological assay of heparin sodium*, Appendix 2.3, and express the results in number of Units per ml.

Storage : Store in tightly-closed containers, sealed so as to exclude micro-organisms, and in a dry place.

Labelling : The label on the container states (1) the number of Units per mg; (2) the date after which the preparation is not intended to be used; (3) the storage conditions; (4) the source of the material as "Heparin Sodium (Lung)" or "Heparin Sodium (Mucous)"

Heparin Sodium Injection

Heparin Injection

Category : Anticoagulant.

Dose : For treatment, by intravenous injection, Heparin Sodium, 20,000 to 50,000 Units daily.

For prophylaxis, by subcutaneous injection, Heparin Sodium, 10,000 to 15,000 Units daily in divided doses.

Usual strengths : 1000, 5000, and 25,000 Units per ml.

Description : Clear, colourless or straw-coloured liquid, free from turbidity and from matter which deposits on standing.

Standards : Heparin Sodium Injection is a sterile solution of Heparin Sodium in Water for Injection. The pH of the solution is adjusted by the addition of a suitable alkali. It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated potency in terms of Heparin Units.

pH : Between 5.0 and 8.0, Appendix 5.10.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using a quantity containing not less than 1000 Units per kg of the rabbit's weight.

Other requirements : Complies with the requirements stated under Injections.

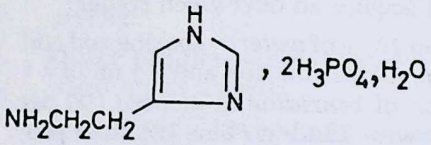
Assay : Carry out the *biological assay of heparin sodium*, Appendix 2.3.

Storage : Store in single-dose or multiple-dose containers in a cool place.

Labelling : The label on the container states (1) the strength as the number of Heparin Units per ml; (2) the organ and the species from which it is derived.

Histamine Acid Phosphate

Histamine Phosphate



$C_5H_9N_3, 2H_3PO_4, H_2O$ Mol. Wt. 325.15

Category : Diagnostic aid (gastric secretion indicator).

Dose : By subcutaneous injection 0.5 to 1 mg; after the administration of an antihistamine, 5 mg.

Description : Long, prismatic, colourless crystals; odourless.

Solubility : Freely soluble in *water*; slightly soluble in *alcohol*.

Standards : Histamine Acid Phosphate is the monohydrate of 2-(4-imidazolyl) ethylamine dihydrogen phosphate. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_5H_9N_3, 2H_3PO_4$, calculated with reference to the anhydrous substance.

Identification : (A) Dissolve 0.1 g in 7 ml of *water* and add 3 ml of *sodium hydroxide solution*; dissolve 50 mg of *sulphanilic acid* in 10 ml of *water* containing two drops of *hydrochloric acid*, and add two drops of a 10 per cent w/v solution of *sodium nitrite*. On mixing the two solutions a deep red colour is produced.

(B) Dissolve 50 mg in 4 ml of hot *water* and add 10 ml of a hot 0.5 per cent w/v solution of *picrolonic acid* in *alcohol (25 per cent)*. The crystalline picrolonate deposited on cooling, after washing with *water* and drying at 105°, melts at about 266°, Appendix 5.11.

(C) A solution (1 in 20) gives the reactions of *phosphates*, Appendix 3.1.

Melting range : Between 130° and 133°, after sintering at about 127°, Appendix 5.11.

Histidine : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using microcrystalline cellulose as the coating substance (Merck, microcrystalline cel-

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

lulose is suitable) and a mixture of 75 volumes of *isopropyl alcohol*, 20 volumes of *ethyl methyl ketone*, and 5 volumes of *strong ammonia solution* as the mobile phase. Apply separately to the plate 5µl of each of two solutions containing (1) 5.0 per cent w/v of the substance being examined and (2) 0.05 per cent w/v of *Dl-histidine monohydrochloride*. After removal of the plate, dry it in a current of warm air, spray with *cadmium and ninhydrin solution*, and heat at 100° for thirty minutes. The spot in the chromatogram obtained with solution (2) is more intense than any corresponding spot in the chromatogram obtained with solution (1).

Water : Between 5.0 and 6.0 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately about 0.16 g and dissolve in 10 ml of *water*. Add 5 ml of *chloroform*, 25 ml of *alcohol*, ten drops of *thymolphthalein solution* and titrate with *0.2N sodium hydroxide*. Each ml of *0.2N sodium hydroxide* is equivalent to 0.01536 g of $C_5H_9N_3, 2H_3PO_4$.

Storage : Store in well-closed, light-resistant containers.

Histamine Acid Phosphate Injection

Histamine Phosphatic Injection

Category : Diagnostic aid (gastric secretion indicator).

Dose : Histamine Acid Phosphate, by subcutaneous injection, 0.5 to 1 mg; after the administration of an antihistamine, 5 mg.

Usual strength : 1 mg in 1 ml.

Description : Clear, colourless solution.

Standards : Histamine Acid Phosphate Injection is a sterile solution of Histamine Acid Phosphate in Water for Injection. It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of $C_5H_9N_3, 2H_3PO_4, H_2O$.

Identification : Evaporate a volume equivalent to about 5 mg of Histamine Acid Phosphate to dryness. The residue complies with **Identification** tests (A) and (C) described under Histamine Acid Phosphate.

pH : Between 3.0 and 6.0, Appendix 5.10.

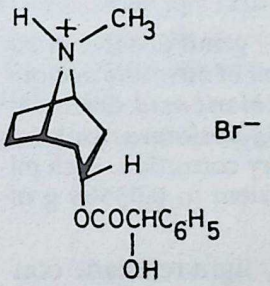
Other requirements : Complies with the requirements stated under Injections.

Assay : Measure accurately a volume equivalent to about 10 mg of Histamine Acid Phosphate and place in a tared 25-ml centrifuge tube containing a thin glass rod slightly curved at the end and add 0.5 ml of *nitranilic acid solution* with continuous stirring, and allow to stand for fifteen minutes. Add 10 ml of *alcohol*, mix and keep at 0° for three hours. Centrifuge for one minute, dislodge any particles at the surface, and again centrifuge for one minute. Decant the supernatant liquid, stir the precipitate with 5 ml of ice-cold *alcohol*. Centrifuge for one and a half minutes, decant and repeat the washing with two further quantities, each of 5 ml of ice-cold *alcohol* and finally with 5 ml of *solvent ether*. Smear the residue over the inside of the tube by means of the glass rod and dry to constant weight at 130°. Each g of residue is equivalent to 0.9529 g of $C_5H_9N_3, 2H_3PO_4, H_2O$.

Storage : Store in single-dose or multiple-dose, light-resistant containers.

Homatropine Hydrobromide

Homatropine Bromide



$C_{16}H_{21}NO_3, HBr$ Mol. Wt. 356.26

Category : Anti-cholinergic (ophthalmic); cycloplegic (ophthalmic).

Description : Colourless, crystalline powder; odourless. Is affected by light.

Solubility : Freely soluble in *water*; sparingly soluble in *alcohol*; slightly soluble in *chloroform*; practically insoluble in *solvent ether*.

Standards : Homatropine Hydrobromide is (1*R*, 3*r*, 5*S*)-3-mandeloyloxytropanium bromide. It contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of $C_{16}H_{21}NO_3$, HBr, calculated with reference to the dried substance.

Identification : (A) A brown precipitate is produced with *iodine solution*.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

(B) To 1 ml of a 1 per cent w/v solution add 1 ml of *dilute ammonia solution*, shake with *chloroform*, and evaporate the chloroform solution to dryness on a water-bath. Warm the residue with 1.5 ml of a 2 per cent w/v solution of *mercuric chloride* in *alcohol (60 per cent)*; a yellow colour, becoming brick-red, is produced (distinction from most other alkaloids except atropine and hyoscyamine).

(C) A solution (1 in 20) gives the reactions of *bromides*, Appendix 3.1.

Melting range : Between 214° and 217°, with partial decomposition, Appendix 5.11.

pH : Between 5.5 and 7.0, determined in a 2.0 per cent w/v solution, Appendix 5.10.

Other alkaloids : A 5 per cent w/v solution does not yield a precipitate with *tannic acid solution*.

Atropine hyoscyamine and hyoscine : To 10 mg add five drops of *nitric acid* and evaporate to dryness in a porcelain dish on a water-bath, add to the residue a few drops of *alcoholic potassium hydroxide solution*; no violet colour is produced.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.3 g and dissolve in 20 ml of *glacial acetic acid*. Add 10 ml of *mercuric acetate solution* and titrate with *0.1 N perchloric acid*, determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.1 N perchloric acid* is equivalent to 0.03563 g of $C_{16}H_{21}NO_3,HBr$.

Storage : Store in well-closed, light-resistant containers.

Hyaluronidase

Category : Enzyme (spreading factor).

Dose : In intravenous therapy, 500 to 1000 Units with each 500 to 1000 ml of infusion fluid. In local anaesthesia, 1000 Units per 20 ml of anaesthetic solution.

Description : White or yellowish-white, fluffy powder; odourless.

Solubility : Very soluble in *water*; practically insoluble in *alcohol*, and in *solvent ether*.

Standards : Hyaluronidase is an enzyme which depolymerises the mucopolysaccharide, hyaluronic acid. It may be prepared from the testes and semen of mammals and purified by fractional precipitation so as to remove most of the inert material; the product is dialysed and dried from the frozen state in single-dose containers, which are sealed so as to exclude micro-organisms to which hydrolysed gelatin or a suitable non-protein stabilising agent may be added. It contains not less than 300 Units per mg and not less than 10,000 Units per mg of tyrosine present.

Identification : (A) A solution containing the equivalent of 100 Units in 1 ml of *saline solution* depolymerises an equal volume of a 1 per cent w/v solution of *sodium hyaluronate* in one minute at 20°. This action is destroyed by heating the hyaluronidase at 100° for thirty minutes.

(B) A solution containing the equivalent of 1 Unit in 0.2 ml of *saline solution* when injected intracutaneously into experimental animals, together with a suitable indicator, shows a spreading activity when compared with a control solution.

pH : Between 4.5 and 7.5, determined in a 0.3 per cent w/v solution, Appendix 5.10.

Clarity and colour of solution : A 1.0 per cent w/v solution in freshly boiled and cooled *water* is clear, and colourless or faintly yellow.

Light absorption : Dissolve a quantity equivalent to 1500 Units in sufficient *carbon dioxide-free water* to produce 5.0 ml and measure the *extinction* of a 1-cm layer at 280 nm and 260 nm, Appendix 5.15A. The *extinction* at 280 nm is not more than 0.6 and the *extinction* at 260 nm is not more than 0.42.

Pyrogens : Complies with *test for pyrogens*, Appendix 2.36, using a quantity containing not less than 250 Units per kg of the rabbit's weight, dissolved in not more than 5 ml of *water for injection*.

Sterility : Complies with the *test for sterility*, Appendix 4.6.

Undue toxicity : A quantity equivalent to 2500 Units dissolved in 0.25 ml *saline solution* and injected subcutaneously into each of five healthy mice, each weighing between 18 to 22 g, does not cause necrosis of the skin or the death of any of them within forty-eight hours; if one of the mice develops necrosis or dies, the test is repeated and the sample complies with the test if none of the second group of five mice develops necrosis or dies within forty-eight hours.

Tyrosine : Transfer the contents of a single container with the aid of a little *water* to a 15-ml centrifuge tube calibrated to 6 ml and evaporate to dryness at 105°. Add 0.2 ml of *6N sodium hydroxide* and heat in saturated steam at 121° for three hours. Cool and add 0.3 ml of *7N sulphuric acid*, 1.5 ml of *water* and 1.5 ml of a 15 per cent w/v solution of *mercuric sulphate* in *5N sulphuric acid*. Heat at 100° for ten minutes, cool and add with shaking

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

1 ml of *7N sulphuric acid* and 1 ml of a 0.2 per cent w/v solution of *sodium nitrite*. Adjust the volume to 6.0 ml with *water*, mix, centrifuge, and decant the supernatant liquid. Twenty minutes after adjusting the volume, measure the *extinction* of the solution at 540 nm, Appendix 5.15 A. Repeat the operation without the hyaluronidase, replacing the 1.5 ml of *water* by 1.5 ml of a solution of *tyrosine* in *0.5N sulphuric acid* containing 30 µg per ml. Calculate the number of micrograms of tyrosine in the amount of hyaluronidase taken by multiplying the ratio of the *extinction* of the first solution to the *extinction* of the second solution by 45.

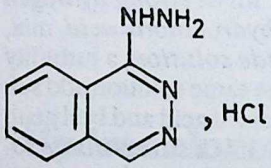
Assay : Carry out the *assay of hyaluronidase*, Appendix 2.6.

Storage : Store in single-dose containers, sealed so as to exclude micro-organisms, in a cool, dry place.

Labelling : The label on the container also states (1) total number of Units contained in it; (2) the animal source of the material; (3) the nature of any added stabilising agent; (4) the date after which the preparation should not be used; (5) that the contents are not intended for intravenous injection.

Hydrallazine Hydrochloride

Hydrallazine Hydrochloride



$C_8H_8N_4, HCl$ Mol. Wt. 196.64

Category : Antihypertensive.

Dose : Oral, 10 mg four times a day, gradually increased upto 50 mg four times a day.

By intramuscular or intravenous injection, 20 to 40 mg, repeated as necessary.

Description : White or almost white crystalline powder; odourless.

Solubility : Soluble in *water*; slightly soluble in *alcohol*; very slightly soluble in *solvent ether*.

Standards : Hydrallazine Hydrochloride is hydrochloride of phthalazin-1-ylhydrazine. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_8H_9ClN_4$, calculated with reference to the dried substance.

Identification : (A) A 0.1 per cent w/v solution gives the reactions of *chlorides*, Appendix 3.1.

(B) The light absorption, in the range 240 to 320 nm, of a 1-cm layer of a 0.001 per cent w/v solution in *0.1N hydrochloric acid* exhibits maxima at about 260 nm and 304 nm; *extinction* at 260 nm, about 0.47 and at 304 nm, about 0.24, Appendix 5.15 A.

Melting range : Between 270° and 280°, with decomposition, Appendix 5.11.

Water-insoluble substances : Not more than 0.5 per cent, determined as follows: Weigh accurately about 2 g and shake by mechanical means with 100 ml of *water* for about thirty minutes. Filter the solution through a sintered-glass crucible and wash into the crucible any undissolved residue remaining in the flask. Wash the residue with three 10-ml portions of *water* and dry at 105° for 3 hours. Cool and weigh the residue.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying "in vacuo" for 8 hours, Appendix 5.8.

Assay : Weigh accurately about 0.15 g in an iodine-flask and dissolve in 25 ml of *water*. Add 25 ml of *hydrochloric acid*, cool to room temperature, add 5 ml of *chloroform*, and titrate with *0.02M potassium iodate* until the purple colour of iodine disappears from the chloroform. Each ml of *0.02M potassium iodate* is equivalent to 0.003933 g of $C_8H_8N_4, HCl$.

Storage : Store in tightly-closed containers.

Hydrochloric Acid

Concentrated Hydrochloric Acid

HCl Mol. Wt. 36.46

Category : Pharmaceutical aid (Acidifying agent).

Description : Clear, colourless, fuming liquid; odour, pungent.

Standards : Hydrochloric Acid is an aqueous solution of hydrogen chloride in water. It contains not less than 35.0 per cent w/w and not more than 38.0 per cent w/w of HCl.

Identification : (A) When neutralised and diluted it gives the reactions of *chlorides*, Appendix 3.1.

(B) When added to *potassium permanganate*, chlorine is evolved.

Arsenic : Not more than 1 part per million, Appendix 3.2.1.

Heavy metals : Not more than 5 parts per million,

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

determined by Method A on a solution prepared in the following manner: Evaporate 3.5 ml to dryness on a water-bath, add 2 ml of *dilute acetic acid* to the residue, add *water* to make 25 ml, Appendix 3.2.4.

Bromide and iodide : Dilute 5 ml with 10 ml of *water*, add 1 ml of *chloroform*, and add drop by drop, with constant shaking, *chlorinated lime solution*; the chloroform layer does not become brown or violet.

Sulphite : Dilute 1 ml with 10 ml of *water*, and add 5 drops of *barium chloride solution* and 0.5 ml of *0.001N iodine*; the colour of the iodine is not completely discharged.

Sulphate : To 5 ml add 10 mg of *sodium bicarbonate* and evaporate to dryness on a water-bath; the residue, dissolved in *water*, complies with the *limit test for sulphates*, Appendix 3.2.8.

Free chlorine : Dilute 5 ml with 10 ml of freshly boiled and cooled *water*, add 1 ml of *potassium iodide solution*, and shake with 1 ml of *chloroform*; the chloroform layer does not become violet within one minute.

Sulphated ash : Not more than 0.01 per cent, Appendix 3.2.7.

Assay : Weigh accurately about 4 g into a stoppered flask containing 40 ml of *water*, and titrate with *N sodium hydroxide*, using *methyl orange solution* as indicator. Each ml of *N sodium hydroxide* is equivalent to 0.03646 g of HCl.

Storage : Store in glass-stoppered containers at a temperature not exceeding 30°

Dilute Hydrochloric Acid

Category : Acidifier.

Dose : 0.6 to 8 ml.

Description : Colourless liquid.

Standards : Dilute Hydrochloric Acid contains not less than 9.5 per w/w and not more than 10.5 per cent w/w of HCl.

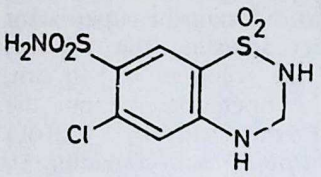
Identification : Complies with **Identification** tests (A) and (B) described under Hydrochloric Acid.

Arsenic; Heavy metals; Bromide and iodide; Sulphate; Free chlorine : Complies with the tests described under Hydrochloric Acid, when three times the quantity is taken for each test.

Assay : Weigh accurately about 10 g and carry out the **Assay** described under Hydrochloric Acid.

Storage : Store in stoppered containers of glass or other inert material, at a temperature below 30°.

Hydrochlorothiazide



$C_7H_8ClN_3O_4S_2$ Mol. Wt. 297.73

Category : Diuretic.

Dose : 25 to 100 mg.

Description : White or almost white, crystalline powder; odourless; taste, slightly bitter.

Solubility : Slightly soluble in *water* and in *alcohol*; insoluble in *chloroform* and in *solvent ether*; soluble in *acetone* and in solutions of alkali hydroxides.

Standards : Hydrochlorothiazide is 6-chloro-3, 4-dihydro-2*H*-1, 2, 4-benzothiadiazine-7-sulphonamide-1, 1-dioxide. It contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of $C_7H_8ClN_3O_4S_2$, calculated with reference to the dried substance.

Identification : (A) Burn 20 mg by the *oxygen-flask method*, Appendix 3.3.6, using 5 ml of *dilute sodium hydroxide solution* as the absorbing liquid. When the process is complete, dilute the liquid to 25 ml with *water*. To 5 ml of the solution so obtained, add 0.1 ml of *strong hydrogen peroxide solution* and 1 ml of *N hydrochloric acid*, mix, and add 0.05 ml of *barium chloride solution*; a turbidity is produced. To a further 5 ml of the same solution add sufficient *dilute sulphuric acid* to make it acid and boil gently for two minutes, cool, add a few ml of *silver nitrate solution*; a white curdy precipitate, soluble in *dilute ammonia solution* but insoluble in *nitric acid* is produced.

(B) Dissolve 13 mg in 10 ml of *0.1N sodium hydroxide*, add sufficient *water* to produce 100 ml, and dilute 10 ml to 100 ml with *0.01N sodium hydroxide*. The light absorption, in the range 230 to 350 nm, of a 1-cm layer of the resulting solution exhibits two maxima at 273 nm and 323 nm; *extinction* at 273 nm, about 0.5, and at 323 nm, about 0.095, Appendix 5.15 A.

(C) Complies with the **Identification** test (B) described under Bendrofluazide, using *hydrochlorothiazide R.S.* instead of *bendrofluazide R.S.*

(D) To 10 mg add 10 mg of *chromatropic acid sodium salt* and 1 ml of *water*, add cautiously 5 ml of *sulphuric acid*, and mix; a purple colour is produced (distinction from chlorothiazide).

Free amine : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel HF 254* as the coating substance and *ethyl acetate* as the mobile

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

phase. Apply separately to the plate 2µl of each of two solutions in *acetone* containing (1) 0.7 per cent w/v of the substance being examined and (2) 0.007 per cent w/v of *4-amino-6-chlorobenzene-1, 3-disulphonamide R.S.* After removal of the plate, dry it in a current of air and reveal the spots as in the **Identification** test (B) described under Bendrofluazide, beginning at the words "spray the dried plate....". The spot in the chromatogram obtained with solution (2) is more intense than any corresponding spot in the chromatogram obtained with solution (1).

Chloride : Shake 1.0 g with 40 ml of *water* for five minutes and filter, the filtrate complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.3 g and dissolve in 50 ml *anhydrous pyridine*. Titrate quickly with *0.1N tetrabutylammonium hydroxide*, determining the end-point potentiometrically and protecting the titrant and the solution from atmospheric carbon dioxide and moisture. Use a glass electrode and a saturated calomel electrode with a saturated solution of *potassium chloride* in *methyl alcohol*. Perform a blank determination and make any necessary correction. Each ml of *0.1N tetrabutylammonium hydroxide* is equivalent to 0.01489 g of $C_7H_8ClN_3O_4S_2$.

Storage : Store in well-closed containers.

Hydrochlorothiazide Tablets

Category : Diuretic.

Dose : Hydrochlorothiazide, 25 to 100 mg daily.

Usual strengths : 25 mg; 50 mg.

Standards : Hydrochlorothiazide Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Hydrochlorothiazide, $C_7H_8ClN_3O_4S_2$.

Identification : Extract a quantity of the powdered tablets equivalent to 50 mg of Hydrochlorothiazide with 20 ml of *acetone*, filter, and evaporate the filtrate to dryness. The residue complies with **Identification** tests (A), (C) and (D) described under Hydrochlorothiazide.

Free amine : Comply with the test described under Hydrochlorothiazide, using as solution (1), a solution prepared in the following manner. Shake a quantity of the powdered tablets equivalent to 70 mg of Hydrochlorothiazide with 50 ml of *acetone*, filter, evaporate the filtrate to dryness, and dissolve the residue in 10 ml of *acetone*.

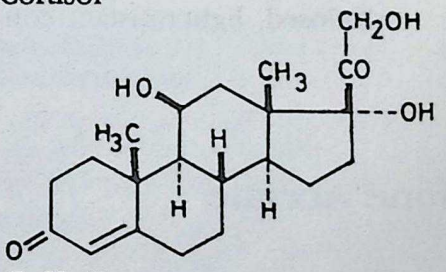
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 25 mg of Hydrochlorothiazide and shake with 75 ml of *acetone*, and allow to stand. Place 5.0 ml of the clear, supernatant liquid in a flask, remove the acetone and boil the residue for one hour with 10 ml of *sodium hydroxide solution* under a reflux condenser. Cool, add 90 ml of *water*, 20 ml of *hydrochloric acid*, and sufficient *water* to produce 200.0 ml. To 10.0 ml of the solution add 1 ml of a 0.5 per cent w/v solution of *sodium nitrite*, mix, and allow to stand for three minutes. Add 1.5 ml of a 1 per cent w/v solution of *sulphamic acid*, shake and allow to stand for three minutes. Add 2.5 ml of a 0.2 per cent w/v solution of *N-(1-naphthyl)-ethylenediamine hydrochloride* in *0.1N hydrochloric acid*, mix and allow to stand for two minutes. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 518 nm, Appendix 5.15 A. Calculate the content of $C_7H_8ClN_3O_4S_2$ from the *extinction* obtained by repeating the operation using 5.0 ml of 0.025 per cent w/v solution of *hydrochlorothiazide R.S.* in *acetone* and beginning at the words "remove the acetone.....", and from the declared content of $C_7H_8ClN_3O_4S_2$ in the *hydrochlorothiazide R.S.*

Storage : Store in well-closed containers.

Hydrocortisone

Cortisol



$C_{21}H_{30}O_5$ Mol. Wt. 362.47

Category : Adrenocortical steriod (anti-inflammatory).

Dose : In the treatment of adrenocortical insufficiency, 10 to 40 mg daily.

Description : White to practically white, crystalline powder; odourless.

Solubility : Practically insoluble in *water*; sparingly soluble in *alcohol* and in *acetone*; slightly soluble in *chloroform*; practically insoluble in *solvent ether*.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Standards : Hydrocortisone in 11β, 17α, 21-trihydroxypregn-4-ene-3,20-dione. It contains not less than 96.0 per cent and not more than the equivalent of 104.0 per cent of $C_{21}H_{30}O_5$, calculated with reference to the dried substance.

Identification : (A) Complies with the *test for identification of steroids*, Appendix 3.3.11, using *solvent I* and *mobile phase A* and applying to the plate 2 µl.

(B) Dissolve 10 mg in 1 ml of *methyl alcohol*, warm, and add 1 ml of *potassium cupri-tartrate solution*; an orange-red precipitate is slowly formed.

(C) Dissolve 1 mg in 1 ml of *sulphuric acid*; a solution having a green fluorescence is produced (distinction from cortisone, prednisone and prednisolone); the solution becomes orange-red and finally dark red.

(D) It melts at about 214°, with decomposition, Appendix 5.11.

Specific optical rotation : Between +150° and +156°, determined in a 1.0 per cent w/v solution in *dioxan*, Appendix 5.12.

Light absorption : *Extinction* of a 1-cm layer of a 0.001 per cent w/v solution in *ethyl alcohol* at the maximum at about 240 nm, between 0.42 and 0.45, Appendix 5.15 A.

Related foreign steroids : Complies with the test for *related foreign steroids, Method A*, Appendix 3.3.12.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

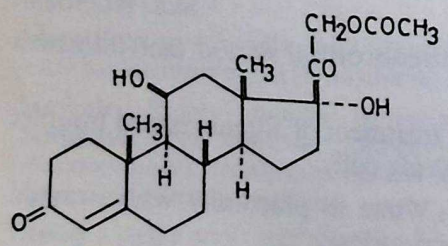
Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Carry out the **Assay** described under Betamethasone, using *hydrocortisone R.S.* for preparing the *standard solution.*

Storage : Store in well-closed, light-resistant containers.

Hydrocortisone Acetate

Cortisol Acetate.



$C_{23}H_{32}O_6$ Mol. Wt. 404.50

Category : Adrenocortical steroid (anti-inflammatory)

Dose : By intra-articular injection or local infiltration, 5 to 50 mg.

Description : Almost white, crystalline powder, odourless.

Solubility : Practically insoluble in *water*; slightly soluble in *alcohol* and in *chloroform.*

Standards : Hydrocortisone Acetate is 11β, 17α, 21-trihydroxypregn-4-ene-3, 20-dione 21-acetate. It contains not less than 96.0 per cent and not more than the equivalent of 104.0 per cent of $C_{23}H_{32}O_6$, calculated with reference to the dried substance.

Identification : (A) Complies with the test for *Identification of steroids*, Appendix 3.3.11, using *solvent I* and *mobile phase B* and applying to the plate 2 µl.

(B) Complies with **Identification** tests (B) and (C) described under Hydrocortisone.

(C) To 50 mg, add 2 ml of *0.5N alcoholic potassium hydroxide*, heat on a water-bath for five minutes, cool, add 2 ml of *sulphuric acid (50 per cent v/v)*, and boil gently for one minute; ethyl acetate is produced.

(D) It melts at about 220°, with decomposition, Appendix 5.11.

Specific optical rotation : Between +158° and +165°, determined in a 1 per cent w/v solution in *dioxan*, Appendix 5.12.

Light absorption : *Extinction* of a 1-cm layer of a 0.001 per cent w/v solution in *ethyl alcohol* at the maximum at about 240 nm, between 0.38 and 0.40, Appendix 5.15 A.

Related foreign steroids : Complies with the test for *related foreign steroids, Method A*, Appendix 3.3.12.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.1 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Carry out the **Assay** described under Betamethasone, using *hydrocortisone acetate R.S.* for preparing the *standard solution.*

Storage : Store in well-closed, light-resistant containers.

Hydrocortisone Acetate Injection

Cortisol Acetate Injection

Category : Adrenocortical steroid (anti-inflammatory).

Dose : Hydrocortisone Acetate. By intra-articular injection, 5 to 50 mg.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Usual strength : 25 mg per ml.

Description : White suspension which settles on standing but readily disperses on shaking.

Standards : Hydrocortisone Acetate Injection is a sterile suspension of a very fine powder of Hydrocortisone Acetate in Sodium Chloride Injection containing suitable dispersing agents. It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of $C_{23}H_{32}O_6$.

Identification : Extract a volume equivalent to 75 mg of Hydrocortisone Acetate with 15 ml of *chloroform* and remove the chloroform from the extract; the residue complies with **Identification** tests (A), (B) and (C) described under Hydrocortisone.

Other requirements : Complies with the requirements stated under Injections.

Assay : Carry out the **Assay** described under Cortisone Injection, using a volume equivalent to 20 mg of Hydrocortisone Acetate. For preparing the *standard solution* use *hydrocortisone acetate R.S.* instead of *cortisone acetate R.S.*

Storage : Store in single-dose or multiple-dose, light-resistant containers.

Labelling : The label on the container states (1) the names of the dispersing agents; (2) "For local injection only"; (3) that the container should be gently shaken before a dose is withdrawn.

Hydrocortisone Eye Ointment

Hydrocortisone Acetate Eye Ointment; Cortisol Acetate Eye Ointment.

Category : Adrenocortical steroid (anti-inflammatory).

Usual strength : 2.5 per cent w/v.

Standards : Hydrocortisone Eye Ointment contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Hydrocortisone Acetate, $C_{23}H_{32}O_6$.

Identification : Boil 2 g with 20 ml of *methyl alcohol*, shake, cool at 0° for thirty minutes, filter, and evaporate the filtrate to dryness. The residue complies with **Identification** tests (A), (B) and (C) described under Hydrocortisone Acetate.

Other requirements : Complies with the requirements stated under Eye Ointments.

Assay : Weigh accurately a quantity equivalent to about 10 mg of Hydrocortisone Acetate and add 30 ml of *aldehyde-free ethyl alcohol.* Heat on a water-bath and mix. Cool and filter into a 100-ml volumetric flask. Repeat the extraction with three further quantities, each of 20 ml, of *aldehyde-free ethyl alcohol.* Mix the extracts, dilute to volume with *aldehyde-free ethyl alcohol* and mix. Dilute 10.0 ml of the resulting solution to 100.0 ml with *aldehyde-free ethyl alcohol* and mix. Transfer 20.0 ml of the resulting solution into a glass-stoppered 50-ml flask and carry out the *assay of steroids*, Appendix 3.3.10, using *hydrocortisone acetate R.S.* for preparing the *standard solution.*

Storage : Store in well-closed, light-resistant containers.

Hydrogen Peroxide Solution

Category : Antiseptic; topical anti-infective.

Description : Colourless liquid; odourless; taste, slightly acid. Rapidly decomposes in contact with oxidisable organic matter and with certain metals and also if allowed to become alkaline.

Standards : Hydrogen Peroxide Solution is an aqueous solution of hydrogen peroxide. It contains not less than 5.0 per cent w/v and not more than 7.0 per cent w/v of H_2O_2, corresponding to about 20 times its volume of available oxygen. It contains not more than 0.025 per cent w/v of a suitable stabilising agent.

Identification : (A) Decomposes with effervescence when made alkaline and heated, evolving oxygen.

(B) To one drop add 2 ml of *dilute sulphuric acid*, shake, add one drop of *potassium chromate solution* and 2 ml of *solvent ether*; the ethereal layer is coloured blue.

Acidity : To 10 ml add 20 ml of *water* and one drop of *methyl red solution* and titrate with *0.1N sodium hydroxide* not less than 0.2 ml and not more than 1 ml of *0.1N sodium hydroxide* is required for neutralisation.

Barium : To 10 ml add 1 ml of *dilute sulphuric acid*; no turbidity is produced.

Stabilising agent : Not more than 0.025 per cent w/v, determined by the following method. Shake 20 ml with successive quantities of 10, 5 and 5 ml of *chloroform.* Evaporate the combined chloroform extracts under reduced pressure and without the aid of heat. Dry the residue at a temperature below 25° over *silica gel.*

Residue on evaporation : Not more than 0.2 per cent w/v, when evaporated on a water-bath in a platinum dish.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

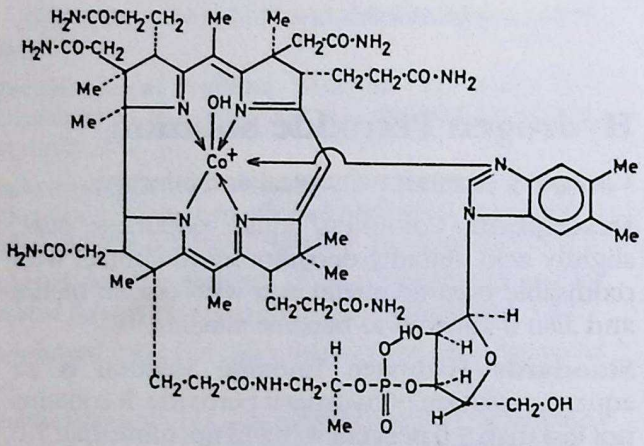
Digitized by Arya Samaj Foundation Chennai and eGangotri

Assay : Dilute 10 ml to 250.0 ml with *water*. To 25.0 ml of the dilution add 5 ml of *5N sulphuric acid* and titrate with *0.1N potassium permanganate* to a permanent pink end-point. Each ml of *0.1N potassium permanganate* is equivalent to 0.001701 g of H_2O_2.

Storage : Store in light-resistant containers, with stoppers resistant to hydrogen peroxide, in a cool place. It should not be stored for long periods.

Labelling : The label on the container states whether or not the solution contains a stabilising agent.

Hydroxocobalamin



$C_{62}H_{89}CoN_{13}O_{15}P$ Mol. Wt. 1346.37

Category : Vitamin B_{12} (haematopoietic).

Dose : In the treatment of megaloblastic anaemia, by intramuscular injection, 1 to 2 mg, in divided doses, in the first week; subsequent doses, 250 micrograms weekly until the blood count is normal; maintenance dose, 1 mg every two months.

Description : Dark red crystals or crystalline powder; almost odourless; almost tasteless.

Solubility : Freely soluble in *water*.

Standards : Hydroxocobalamin is α-(5, 6-dimethylbenzimidazol-2-yl) hydroxocobamide. It occurs either as aquocobalamin chloride [Coa-{a-(5,6-dimethylbenzimidazolyl)}-Coβ-aquocobamide chloride], which contains not less than 96.0 per cent of $C_{62}H_{90}ClCoN_{13}O_{15}P$, or as aquocobalamin sulphate, which contains not less than 96.0 per cent of $C_{124}H_{180}Co_2N_{26}O_{34}P_2S$, both calculated with reference to the dried substance.

Identification : (A) Measure the *extinction* of the solution used in the **Assay** in a 1-cm cell at the maxima at about 274, 351 and 525 nm, Appendix 5.15 A. The ratios of the *extinctions* at 274 nm and 525 nm to the *extinction* at 351 nm are about 0.8 and about 0.3 respectively.

(B) Complies with **Identification** test (B) described under Cyanocobalamin.

(C) A solution (1 in 20) gives the reactions of *chlorides*, or of *sulphates*, Appendix 3.1.

Coloured impurities : Not more than 5.0 per cent, when determined by the following method:

Protect the solution from light throughout the test. Shake together 500 ml of *water* and 500 ml of *s-butyl alcohol* and allow to stand overnight at 25° to 30°. Carry out the method for *descending paper chromatography*, Appendix 5.4.2. Use as the stationary phase, the lower layer of the solvents with the addition of 1 per cent v/v of *acetic acid* and 0.5 g of *potassium cyanide* and as the mobile phase, the upper layer with the addition of 5 per cent v/v of *s-butyl alcohol* and 1 per cent v/v of *acetic acid*. Weigh accurately about 2 mg and dissolve in 1 ml of *water*, add 0.05 ml of *hydrocyanic acid solution* and allow to stand for fifteen minutes. Apply the solution to the paper (which should be 22.5 cm wide, leaving 2.5 cm clear at both ends) in successive streaks, drying each application in a current of *nitrogen* without the aid of heat. Insert the paper in the tank and allow to stand for not less than four hours. Elute until the hydroxocobalamin has travelled about two-thirds of the length of the paper.

From the dried paper, cut out and discard the main band, trim the remaining pieces of paper of any uncoloured zones at the top and bottom, fasten together the vertical edges of each of the two remaining strips, and allow the cylinders so obtained to stand on filter paper moistened with *water* until the coloured material reaches the top edges. Remove the uncoloured paper, elute the coloured material by descending chromatography with the minimum quantity of *water*, combine the eluates, dilute to a suitable volume with *water*, filter through a sintered-glass filter, and measure the *extinction* of the filtrate at the maximum at about 361 nm, Appendix 5.15 A, using as the blank the solution obtained by repeating the procedure without the hydroxocobalamin; make the cylinders from pieces of the paper of the same size and cut from the same positions as those used for the test solution. E(1 per cent, 1-cm) of the coloured impurities at the maximum at about 361 nm is 207.

Other cobalamins : Not more than 3.0 per cent when determined by the following method: Slurry 10 g of diethylaminoethylcellulose (Whatman DE 23 is suitable) with 150 ml of *0.5N hydrochloric acid* for one hour, filter, and wash with *water* until the pH of the washings is above 4.5. Slurry the cellulose with 150 ml of *0.5N sodium hydroxide* for one hour, filter and wash with *water* until the pH of the washings is 7 to 7.5. With the aid of 1000 ml of *water*, transfer the slurry in portions to a glass column 22 cm long and 1.2 cm in internal diameter, fitted with a sintered glass disc and a tap. Allow to settle

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

until the height of the absorbent is about 19 cm, wash with *water* until the pH of the effluent is constant and tamp down to a height of about 15.5 cm.

Prepare a second column in exactly the same way using Carboxymethylcellulose (Whatman CM 23 is suitable) in place of the diethylaminoethylcellulose, but reversing the order of the acid and alkali treatment. Tamp down the column to a height of about 10 cm.

Place a plug of glass wool on each column and allow to drain until only a small amount of water remains above the column. Support the columns so that the effluent from the diethylaminoethylcellulose column runs into the carboxymethylcellulose column.

Weigh accurately about 50 mg of hydroxocobalamin, and dissolve in 20 ml of *water* containing sufficient *hydrochloric acid* to give a pH below 4.0. Add the solution to the diethylaminoethylcellulose column and allow to run through both columns, rejecting the first colourless eluate. Elute with *water* and collect 50 ml of the coloured eluate from the carboxymethylcellulose column. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 361 nm, Appendix 5.15 A. Calculate the content of other cobalamins, taking 207 as the value of E(1 per cent, 1-cm) at the maximum at about 361 nm.

Acidic impurities : Not more than 3.0 per cent when determined by the following method: Elute the diethylaminoethylcellulose column used in the test for **Other cobalamins** with a 1 per cent w/v solution of *sodium chloride*, collecting 50 ml of the eluate. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum between 351 and 361 nm, Appendix 5.15 A. Calculate the content of acidic impurities taking 190 as the value of E (1 per cent, 1-cm) at the maximum between 351 and 361 nm.

Loss on drying : Between 8.0 per cent and 12.0 per cent (aquocobalamin chloride) and between 8.0 per cent and 16.0 per cent (aquocobalamin sulphate), determined on 1.0 g by drying "in vacuo at 105°", Appendix 5.8.

Assay : Protect the solutions from light throughout the assay.

Weigh accurately about 25 mg and dissolve in sufficient of a solution containing 0.8 per cent v/v of *glacial acetic acid* and 1.09 per cent w/v of *sodium acetate* to produce 1000.0 ml. Measure the *extinction* of the resulting solution at the maximum at about 351 nm, Appendix 5.15 A. Calculate the content of $C_{62}H_{90}ClCoN_{13}O_{15}P$ or $C_{124}H_{180}Co_2N_{26}O_{34}P_2S$ taking 190 or 188, respectively as the value of E(1 per cent, 1-cm) at the maximum at about 351 nm.

Storage : Store in tightly-closed, light-resistant containers, and in a cool place.

Labelling : The label on the container states whether the containers are aquocobalamin chloride or aquocobalamin sulphate.

Hydroxocobalamin Injection

Category : Vitamin B_{12} (haematopoietic).

Dose : Hydroxocobalamin. In the treatment of megaloblastic anaemia, by intramuscular injection, 1 to 2 mg in divided doses, in the first week; subsequent doses, 250 mcg weekly until the blood count is normal; maintenance dose, 1 mg every two months.

Usual strengths : 500 µg per ml; 1000 µg per ml.

Standards : Hydroxocobalamin Injection is a sterile solution of Hydroxocobalamin in Water for Injection, containing sufficient Acetic Acid or Hydrochloric Acid to adjust the pH to 4.0. It contains not less than 95.0 per cent and not more than 110.0 per cent of the stated amount of hydroxocobalamin, $C_{62}H_{89}CoN_{13}O_{15}P$.

Identification : Measure the *extinction* at 351 nm and 361 nm, Appendix 5.15 A. The ratio of the *extinction* at 361 nm to that at 351 nm is about 0.65.

pH : Between 3.8 and 5.5, Appendix 5.10.

Coloured impurities : Protect the solutions from light throughout the test.

Measure accurately a volume equivalent to about 2 mg of anhydrous hydroxocobalamin and add, for each 2 ml taken, 0.05 ml of *hydrocyanic acid solution*; allow to stand for fifteen minutes, and extract with three or more quantities, each of 1 ml, of a mixture of equal parts of *phenol* and *chloroform*, until the aqueous layer is no longer red. To the combined extracts add 15 ml of *acetone* and 80 ml of *solvent ether*, mix, centrifuge, and decant the ether layer. Continue the washings with further quantities, each of 50 ml, of *solvent ether*, decanting and evaporating the ether layers until the odour of phenol is no longer perceptible. Dissolve the residue in the centrifuge tube in the minimum quantity of *water* and complete the test for **Coloured impurities** described under Hydroxocobalamin. The content of coloured impurities is not more than 15 per cent of the content of anhydrous hydroxocobalamin determined in the **Assay** and the difference between these contents is not less than 85 per cent of the stated content of anhydrous hydroxocobalamin.

Other requirements : Complies with the requirements stated under Injections.

Assay : Dilute an accurately measured volume equivalent to about 4 mg of anhydrous hydroxocobalamin to 200.0 ml with a solution containing 0.8 per cent v/v of *glacial acetic acid* and 1.90 per cent w/v of *sodium acetate* and measure the *extinction* of 1-cm layer of the resulting solution at the maximum at about 351 nm, Appendix 5.15 A. Calculate the content of $C_{62}H_{89}CoN_{13}O_{15}P$ taking 195 as the value of E(1 per cent, 1-cm) at the maximum at about 351 nm.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

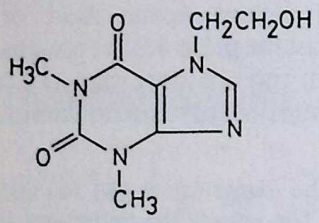
Digitized by Arya Samaj Foundation Chennai and eGangotri

Storage : Store in light-resistant containers.

Labelling : The label on the container states the strength in terms of the equivalent amount of anhydrous hydroxocobalamin in a suitable dose volume.

Hydroxyethyltheophylline

Etofylline



$C_9H_{12}N_4O_3$ Mol. Wt. 224.22

Category : Smooth muscle relaxant (bronchiolar).

Dose : 100 to 300 mg by mouth or by intravenous or intramuscular injection.

Description : White, crystalline powder; odourless; taste, bitter.

Solubility : Soluble in *water*; sparingly soluble in *chloroform*; slightly soluble in *alcohol*; insoluble in *solvent ether*.

Standards : Hydroxyethyltheophylline is 7-(2-hydroxyethyl)-1, 3-dimethyl-(1*H*, 3*H*)-purine-2, 6-dione. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_9H_{12}N_4O_3$, calculated with reference to the dried substance.

Identification : (A) Mix a few mg with five drops of *strong hydrogen peroxide solution* and five drops of *dilute hydrochloric acid*. Heat to dryness on a water-bath. Cool and add one drop of *dilute ammonia solution*; the yellow-red colour of the residue changes to red-violet.

(B) Dissolve 1 g in 5 ml of *acetic anhydride* and heat under a reflux condenser for 15 minutes. Cool and add a mixture of 5 ml of *methyl alcohol* and 50 ml of *solvent ether*. Cool in ice-water for a few minutes. Filter and wash the precipitate with a few ml of *solvent ether*. Recrystallise from *alcohol* and dry the crystals "in vacuo". The crystals melt at about 100°, Appendix 5.11.

Melting range : Between 161° and 166°, Appendix 5.11.

Acidity or Alkalinity : Dissolve 0.5 g in 10 ml of *carbon dioxide-free water* and add 0.25 ml of *bromothymol blue solution*. Titrate with *0.02N sodium hydroxide* till the solution turns blue. Nor more than 0.2 ml is required.

Theophylline : Dissolve 2.0 g in 10 ml of hot *water*. Add 0.25 ml of *bromothymol blue solution* and 5 ml of *0.1N silver nitrate*. Titrate with *0.1N sodium hydroxide* to a blue colour. Not more than 0.25 ml is required.

Related impurities : Carry out the method for *thin-layer chromatography*. Appendix 5.4.3, using *silica gel HF254* as the coating substance and a mixture of 90 volumes of *chloroform*, 10 volumes of *alcohol* and 1 volume of *strong ammonia solution* as the mobile phase. Apply separately to the plate 10 µl of each of two freshly prepared solutions containing (1) 3.0 per cent w/v of the substance being tested, in a mixture of 60 volumes of *methyl alcohol* and 40 volumes of *water* and (2) 1.0 ml of solution (1) diluted to 100 ml with *methyl alcohol*. After removal of the plate, allow the solvent to evaporate at room temperature and examine under an ultra-violet lamp having a maximum output at about 254 nm. The chromatogram obtained with solution (1) may show, in addition to the principal spot, at most, three secondary spots. None of the secondary spots is more intense than the spot in the chromatogram obtained with solution (2).

Chloride : 1.0 g dissolve in 25 ml of *water* complies with the *limit test for chlorides*, Appendix 3.2.2.

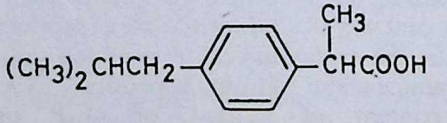
Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 100° to 105°, Appendix 5.8.

Assay : Weigh accurately about 0.3 g and dissolve in 3.0 ml of *anhydrous formic acid*. Add 50 ml of *acetic anhydride* and titrate with *0.1N perchloric acid*, determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02242 g of $C_9H_{12}N_4O_3$.

Storage : Store in well-closed containers.

Ibuprofen



$C_{13}H_{18}O_2$ Mol. Wt. 206.28

Category : Analgesic and anti-inflammatory.

Dose : 0.6 g to 1.2 g daily, in divided doses.

Description : White or almost white powder or crystals; odour, characteristic.

Solubility : Practically insoluble in *water*; freely soluble in *alcohol*, in *chloroform*, in *solvent ether*

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

and in *acetone*; soluble in aqueous solutions of alkali hydroxides and carbonates.

Standards : Ibuprofen is 2-(4-isobutylphenyl) propionic acid. It contains not less than 98.5 per cent of $C_{13}H_{18}O_2$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *ibuprofen R.S.*, Appendix 5.15 B.

(B) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.025 per cent w/v solution in *0.1N sodium hydroxide*, exhibits maxima at 264 nm and 273 nm, and a less well-defined maximum at 259 nm; *extinction* at 264 nm, about 0.47 and at 273 nm, about 0.39, Appendix 5.15 A.

Melting range : Between 75° and 78°, Appendix 5.11.

Related compounds : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel H* as the coating substance and a mixture of 15 volumes of *n-hexane*, 5 volumes of *ethyl acetate* and 1 volume of *glacial acetic acid* as the mobile phase. Apply separately to the plate 5 µl of each of two solutions in *chloroform* containing (1) 10 per cent w/v of the substance being examined, (2) 0.1 per cent w/v of *ibuprofen R.S.* After removal of the plate, allow it to dry in air, spray very lightly with a 1 per cent w/v solution of *potassium permanganate* in *dilute sulphuric acid*, heat at 120° for twenty minutes and examine under an ultra-violet lamp having a maximum output at about 366 nm. Any spot in the chromatogram obtained with solution (1), other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (2).

Heavy metals : Not more than 10 parts per million, determined on 2.0 g by Method B, Appendix 3.2.4.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss of drying : Not more than 0.5 per cent, determined on 1.0 g by drying "in vacuo", Appendix 5.8.

Assay : Weigh accurately about 0.5 g and dissolve in 100 ml of *alcohol*, previously neutralised to *phenolphthalein solution*, titrate with *0.1N sodium hydroxide*, using *phenolphthalein solution* as indicator. Each ml of *0.1N sodium hydroxide*, is equivalent to 0.02063 g of $C_{13}H_{18}O_2$.

Storage : Store in well-closed containers.

Ibuprofen Tablets

Category : Analgesic and anti-inflammatory.

Dose : Ibuprofen, 0.6 to 1.2 g daily, in divided doses.

Usual strength : 0.2 g.

Standards : Ibuprofen Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Ibuprofen, $C_{13}H_{18}O_2$. The tablets may be coated.

Identification : Extract a quantity of the powdered tablets equivalent to 0.5 g of Ibuprofen with 20 ml of *acetone*; filter and evaporate the filtrate to dryness, without heating, with the aid of a current of air. The residue, after recrystallisation, melts at about 75°, Appendix 5.11, and complies with **Identification** test (A) described under Ibuprofen.

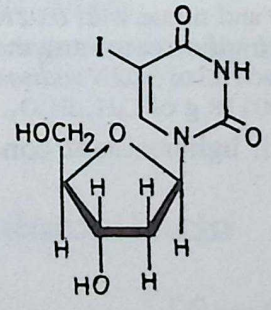
Related compounds : Comply with the test for **Related compounds** described under Ibuprofen using as solution (1) a solution prepared in the following manner. Extract a quantity of the powdered tablets equivalent to 0.2 g of Ibuprofen with three quantities, each of 10 ml, of *chloroform* and filter; evaporate the combined filtrates to about 1 ml and add sufficient *chloroform* to produce 2.0 ml. Disregard any spot with an R_f relative to Ibuprofen of about 1.2.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.5 g of Ibuprofen and extract with 20 ml of *chloroform*, filter, and wash the powder and filter with three quantities, each of 10 ml, of *chloroform*. Evaporate the combined filtrates to dryness by gentle heating, with the aid of a current of air, and carry out the **Assay** described under Ibuprofen.

Storage : Store in tightly-closed containers.

Idoxuridine



$C_9H_{11}IN_2O_5$ Mol. Wt. 354.10

Category : Antiviral agent (topical).

Description : Colourless crystals or white, crystalline powder; odourless; tasteless.

Solubility : Slightly soluble in *water*, and in *alcohol*; practically insoluble in *chloroform* and in *solvent ether*.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Standards : Idoxuridine is 5-iodo-2′-deoxyuridine. It contains not less than 97.0 per cent and not more than the equivalent of 101.0 per cent of $C_9H_{11}IN_2O_5$, calculated with reference to the dried substance.

Identification : (A) On heating, iodine vapours are evolved.

(B) The light absorption in the range 230 to 350 nm, of a 1-cm layer of a 0.004 per cent w/v solution in *0.01N sodium hydroxide*, exhibits a maximum only at 279 nm; *extinction* at 279 nm, about 0.65, Appendix 5.15 A.

Specific optical rotation : Between +28° and +32° at 20°, determined in a 1.0 per cent w/v solution in *N sodium hydroxide*, Appendix 5.12.

Inorganic iodide : Dissolve 0.25 g in a mixture of 25 ml of *water* and 2.5 ml of *N sodium hydroxide*, add 10 ml of *N hydrochloric acid* and sufficient *water* to produce 50 ml, mix and filter. To 25 ml of the filtrate, add 2.5 ml of *hydrogen peroxide solution*, and extract with 10 ml of *chloroform*. Any pink colour produced in the chloroform layer is not darker than that produced by treating 0.275 mg of *potassium iodide* in the same manner.

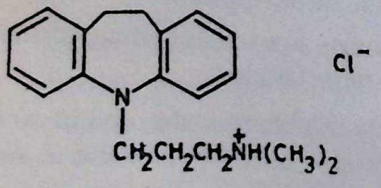
Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying "in vacuo at 60°" for two hours, Appendix 5.8.

Assay : Carry out the *oxygen-flask method*, Appendix 3.3.6, using about 20 mg, accurately weighed, and a mixture of 10 ml of *water* and 2 ml of *N sodium hydroxide* as the absorbing liquid. When the process is complete, add to the flask an excess (5 ml to 10 ml) of *acetic bromine solution*, and allow to stand for two minutes. Remove the excess of bromine by the addition of *formic acid* (0.5 ml to 1 ml), rinse the sides of the flask with *water*, and sweep out any bromine vapour above the liquid with a current of air. Add 1 g of *potassium iodide* and titrate with *0.02N sodium thiosulphate*, using *starch solution*, towards the end of the titration, as indicator. Each ml of *0.02N sodium thiosulphate* is equivalent to 0.00118 g of $C_9H_{11}IN_2O_5$.

Storage : Store in well-closed, light-resistant containers.

Imipramine Hydrochloride



$C_{19}H_{24}N_2$, HCl Mol. Wt. 316.87

Category : Antidepressant.

Dose : 50 to 150 mg daily, in divided doses.

Description : White or slightly yellow crystalline powder; almost odourless; taste burning, followed by a sensation of numbness.

Solubility : Freely soluble in *water*, in *alcohol*, and in *chloroform*; practically insoluble in *solvent ether*.

Standards : Imipramine Hydrochloride is 3-[10,11-dihydro-5*H*-dibenz (*b,f*) azepin-5-yl]propyldimethylammonium chloride. It contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of $C_{19}H_{24}N_2$, HCl, calculated with reference to the dried substance.

Identification : (A) Dissolve about 5 mg in 2 ml of *nitric acid*; an intense blue colour is produced.

(B) Dissolve 0.5 g in 20 ml of *alcohol*, heat to boiling, add 5 ml of a saturated solution of *picric acid* in *alcohol* and allow to cool. The precipitate after washing with *alcohol* and drying, melts at about 140°, Appendix 5.11.

(C) Dissolve 50 mg in 3 ml of *water* and add one drop of a 2.5 per cent w/v solution of *quinhydrone* in *methyl alcohol*; no red colour is produced within fifteen minutes (distinction from desipramine).

(D) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

Melting range : Between 170° to 174°, Appendix 5.11.

Light absorption : The light absorption, in the range 230 to 350 nm of a 1-cm layer of 0.0015 per cent w/v solution in *0.1N hydrochloric acid* exhibits a maximum at about 250 nm; *extinction* at 250 nm, 0.38 to 0.40, Appendix 5.15 A.

pH : Between 4.2 and 5.2, determined in a 10 per cent w/v solution, Appendix 5.10.

Heavy metals : Not more than 10 parts per million, determined by Method B on 2.0 g, Appendix 3.2.4.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 55 volumes of *ethyl acetate*, 35 volumes of *glacial acetic acid*, 5 volumes of *hydrochloric acid* and 5 volumes of *water* as the mobile phase but allowing the solvent front to ascend 12 cm above the line of application. Apply separately to the plate 5 µl of each of two freshly prepared solutions in *alcohol* containing (1) 2.0 per cent w/v of the substance being examined and (2) 0.0040 per cent w/v of the substance being examined. After removal of the plate, allow the solvent to evaporate for five minutes and spray with a 0.5 per cent w/v solution of *potassium dichromate*

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

in a mixture of 1 volume of *sulphuric acid* and 4 volumes of *water*. Any spot in the chromatogram obtained with solution (1), other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (2).

Iminodibenzyl : Dissolve 50 mg in 10 ml of a mixture of equal volumes of *hydrochloric acid* and *alcohol* and whilst cooling add 5 ml of a 0.4 per cent v/v solution of *furfuraldehyde* in *alcohol* and 5 ml of *hydrochloric acid*. Keep the mixture at 25° for 3 hours, protected from light. Dilute to 20 ml with a mixture of equal volumes of *hydrochloric acid* and *alcohol* and immediately measure the *extinction* of the resulting solution at the maximum at about 565 nm, Appendix 5.15 A, using as the blank a mixture prepared in the same manner but without the substance being examined; the *extinction* is not greater than 0.2.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.3 g, dissolve in 80 ml of *glacial acetic acid*, add 10 ml of *mercuric acetate solution* and titrate with *0.1N perchloric acid*, using *crystal-violet solution* as the indicator. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.03169 g of $C_{19}H_{24}N_2$, HCl.

Storage : Store in tightly-closed, light-resistant containers.

Imipramine Tablets

Category : Antidepressant.

Dose : Imipramine Hydrochloride, 75 to 150 mg daily in divided doses.

Usual strengths : 10 mg; 25 mg.

Standards : Imipramine Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Imipramine Hydrochloride, $C_{19}H_{24}N_2$, HCl. The tablets may be coated.

Identification : Triturate a quantity of the powdered tablets equivalent to about 0.25 g of Imipramine Hydrochloride with 10 ml of *chloroform*, filter, evaporate the filtrate to low bulk, add *solvent ether* until a turbidity is produced, and allow to stand. The precipitate, after recrystallisation from *acetone*, melts at about 172°, Appendix 5.11, and complies with **Identification** tests (A), (C) and (D) described under Imipramine Hydrochloride.

Related substances : Comply with the test described under Imipramine Hydrochloride, using for solution (1), a solution prepared as follows. Shake a quantity of the powdered tablets equivalent to 0.2 g of Imipramine Hydrochloride with three quantities, each of 10 ml, of *chloroform* and filter; evaporate the combined filtrates to dryness and dissolve the residue in 10 ml of *methyl alcohol* containing 1 ml of *strong ammonia solution*. Use for solution (2) a 0.006 per cent w/v solution of *iminodibenzyl R.S.* in *methyl alcohol*.

Uniformity of content (for 10 mg tablets only) : Powder one tablet, shake with 25 ml of *0.1N hydrochloric acid* for thirty minutes, add sufficient *0.1N hydrochloric acid* to produce 100.0 ml, and filter. Dilute 5.0 ml of the filtrate to 50.0 ml with *0.1N hydrochloric acid*, and measure the *extinction* of the resulting solution at the maximum at about 250 nm, Appendix 5.15 A. Calculate the content of $C_{19}H_{24}N_2$, HCl, taking 264 as the value of E(1 per cent, 1-cm) at the maximum at about 250 nm.

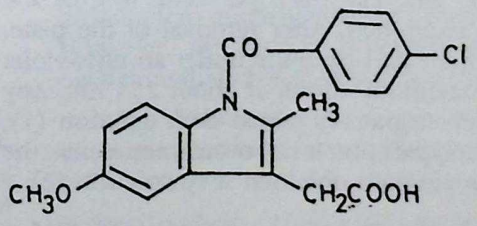
Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 85 and 115 per cent of the average except that for one tablet the content may be between 80 and 120 per cent of the average.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 75 mg of Imipramine Hydrochloride, shake with 100 ml of *0.1N hydrochloric acid* for thirty minutes, add sufficient *0.1N hydrochloric acid* to produce 250.0 ml and filter. Dilute 5.0 ml to 100.0 ml with *0.1N hydrochloric acid* and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 250 nm, Appendix 5.15 A. Calculate the content of $C_{19}H_{24}N_2$, HCl taking 264 as the value of E(1 per cent, 1-cm) at the maximum at about 250 nm.

Storage : Store in tightly-closed containers.

Indomethacin



$C_{19}H_{16}ClNO_4$ Mol. Wt.-357.79

Category : Anti-inflammatory and analgesic.

Dose : 75 to 100 mg daily, in divided doses.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Description : Pale yellow to brownish-yellow, crystalline powder; odourless or almost odourless; almost tasteless.

Solubility : Practically insoluble in *water*; sparingly soluble in *alcohol*, in *chloroform*, and in *solvent ether*.

Standards : Indomethacin is 1-(4-chlorobenzoyl)-5-methoxy-2-methyl-3-indolylacetic acid. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_{19}H_{16}ClNO_4$, calculated with reference to the dried substance.

Identification : (A) Dissolve 0.3 g in 15 ml of *methyl alcohol*. To 5 ml of this solution add 0.1 g of *sodium hydroxide*, shake, and allow to stand for five minutes; the colour of the solution changes from yellow to greenish-yellow and finally to very pale yellow. To another 5 ml of the alcoholic solution add 2.5 ml of *hydrochloric acid*; a white precipitate is produced and the supernatant liquid becomes very pale yellow.

(B) Dissolve 0.1 g in 100 ml of *water* containing 0.5 ml of *dilute sodium hydroxide solution*. To 1 ml of the solution add 1 ml of a 0.1 per cent w/v solution of *sodium nitrite*, allow to stand for five minutes, and add 0.5 ml of *sulphuric acid*; a deep yellow colour is produced. To another 1 ml of the solution add 1 ml of the sodium nitrite solution, allow to stand for five minutes, and add 0.5 ml of *hydrochloric acid*; a green colour is produced.

(C) The light absorption, in the range 300 to 350 nm, of a 1-cm layer of a 0.0025 per cent w/v solution in a mixture of 1 volume of *N hydrochloric acid* and 9 volumes of *methyl alcohol*, exhibits a maximum only at 318 nm, *extinction* at 318 nm, about 0.45, Appendix 5.15 A.

Melting range : Between 158° and 162°, Appendix 5.11.

Foreign substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using as the coating substance a suspension of *silica gel HF 254* in a 4.7 per cent w/v solution of *sodium dihydrogen phosphate*. Use a mixture of 70 volumes of *solvent ether* and 30 volumes of *light petroleum (boiling range, 40° to 60°)* as the mobile phase. Apply separately to the plate 10 µl of each of two freshly prepared solutions in *methyl alcohol* containing (1) 2.0 per cent w/v of the substance being examined, and (2) 0.01 per cent w/v of the substance being examined. After removal of the plate, allow it to dry in air and examine under an ultra-violet lamp having a maximum output at about 254 nm. Any spot in the chromatogram obtained with solution (1), other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (2).

Alkaline hydrolysis : Weigh accurately about 0.45 g and dissolve in 25.0 ml of *methyl alcohol* through which *carbon dioxide-free nitrogen* has previously been passed for fifteen minutes. While passing the *nitrogen* through the solution, add 5.0 ml of *N sodium hydroxide (carbonate-free)*, mix and stopper immediately. Allow to stand for fifteen minutes. Again pass the nitrogen through the solution, add 30 ml of *carbon dioxide-free water*, close the flask, and allow to stand for ninety minutes, stirring if necessary to obtain a clear solution. Wash the stopper and sides of the flask with 50 ml of *carbon dioxide-free water* and titrate with *0.1N hydrochloric acid*, using *phenolphthalein solution* as indicator and maintaining a constant stream of the nitrogen through the solution.

Repeat the operation without the Indomethacin. Calculate the volume of *0.1N sodium hydroxide* required by 1 g of Indomethacin in the test and the volume required by 1 g of Indomethacin in the **Assay**. The difference between the volumes is not less than 27.25 ml and not more than 28.25 ml.

Heavy metals : Not more than 20 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

Sulphated ash : Not more than 0.2 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying "in vacuo at 100°" for 2 hours, Appendix 5.8.

Assay : Weigh accurately about 0.45 g and dissolve in 75 ml of *methyl alcohol* through which *carbon dioxide-free nitrogen* has previously been passed for fifteen minutes. Maintaining a constant stream of the nitrogen through the solution, add 75 ml of *carbon dioxide-free water* and titrate with *0.1N sodium hydroxide* (*carbonate-free*) using *phenolphthalein solution* as indicator. Repeat the operation without the indomethacin. The difference between the titrations represent the amount of alkali required by the indomethacin. Each ml of *0.1N sodium hydroxide* is equivalent to 0.03578 g of $C_{19}H_{16}ClNO_4$.

Storage : Store in well-closed, light-resistant containers.

Indomethacin Capsules

Category : Anti-inflammatory and analgesic.

Dose : Indomethacin, 75 to 100 mg daily, in divided doses.

Usual strength : 25 mg.

Standards : Indomethacin Capsules contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Indomethacin. $C_{19}H_{16}ClNO_4$.

Identification : (A) Mix a quantity of the contents of the capsules equivalent to 25 mg of Indomethacin with 2 ml of *water*, and add 2 ml of *dilute sodium hydroxide*

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

solution. A bright yellow colour is produced which fades rapidly.

(B) Complies with **Identification** test (B) described under Indomethacin, using the filtrate obtained by shaking a quantity of the contents of the capsules equivalent to 0.1 g of Indomethacin with a mixture of 100 ml of *water* and 0.5 ml of *dilute sodium hydroxide solution*, and filtering.

Other requirements : Comply with the requirements stated under Capsules.

Assay : Weigh accurately a quantity of the mixed contents of 20 capsules equivalent to 50 mg of Indomethacin, add 10 ml of *water* and allow to stand for ten minutes with occasional swirling. Add 75 ml of *methyl alcohol*, shake well and add sufficient *methyl alcohol* to produce 100.0 ml. To 5.0 ml add sufficient of mixture of equal volumes of *methyl alcohol* and *buffer solution, pH 7.2* to produce 100.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 318 nm, Appendix 5.15 A. Calculate the content of $C_{19}H_{16}ClNO_4$, taking 193 as the value of E(1 per cent, 1-cm) at the maximum at about 318 nm.

Storage : Store in tightly-closed containers.

Injections

Injectable Preparations

NOTE—The provisions of this monograph do not necessarily apply to Blood Products or Immunological Products because of their special nature and licensing requirements.

Injections are sterile products containing one or more medicaments intended for administration into the body tissues. They include intravenous infusions and powders for injections.

Injections should be prepared by methods designed to ensure their sterility to avoid contamination with micro-organisms and foreign material and to ensure the absence of pyrogens.

Preparation of Injections

1. Vehicles : Injections which are solutions or suspensions require vehicles in which the medicament or medicaments are incorporated. In aqueous injections, unless otherwise specified in the individual monograph the most commonly used vehicle is Water for Injection. Where the use of Water for Injection is directed, water freshly prepared by the process described under Water for Injection may be used, the sterilisation at this stage being omitted, provided that the final product is immediately sterilised. Where the use of Water for Injection free from dissolved air or from dissolved carbon dioxide is specified, water freshly prepared by the process described under Water for Injection is boiled for at least ten minutes with as little exposure to air as possible, cooled with precautions to exclude air and carbon dioxide, and sterilised by heating in an autoclave. Vehicles for aqueous Injections pass the *test for pyrogens*, Appendix 2.36.

Fixed oils and esters such as ethyl oleate may be used as vehicles for non-aqueous injections. Fixed oils are of vegetable origin, colourless or nearly so, and have no odour or taste suggestive of rancidity.

Any other suitable vehicles may be used, provided they are safe in the volume of injections administered and also provided they do not interfere with the therapeutic efficacy of the preparation or with its response to the prescribed assays and tests of the pharmacopoeia.

2. Added substances : Suitable substances may be added to injectable preparations to increase stability or usefulness, unless otherwise indicated in the individual monograph. At the concentration at which they are used, such substances should be harmless, should not adversely affect the medicinal action of the preparation and should not interfere with the responses to the specified assays and tests. No colouring agent may be added, solely for the purpose of colouring the finished preparation intended for parenteral administration.

Isotonic solutions—Aqueous Injections for administration by the subcutaneous, intradermal, intramuscular, or in the case of large volumes, intravenous route, should if possible be made isotonic with blood by the addition of Sodium Chloride or other suitable substances.

Buffering agents—Buffering agents should not be used in preparations intended for intraocular or intracardiac injections, or in products which will gain access to the cerebrospinal fluid.

Preservatives—A suitable substance or mixture of substances to prevent the growth of micro-organisms must be added to preparations intended for injections that are packaged in multi-dose containers, regardless of the method of sterilisation employed, unless otherwise directed in the individual monograph, or unless the active ingredients are themselves bacteriostatic. Such substances are used in concentrations that will prevent the growth of or kill micro-organisms in the preparations for injections. However, sterilisation processes should be employed even though such substances are used.

Other substances—In some injections the air in the container may be evacuated or be displaced by a chemically inert gas.

3. Sterilisation : Methods of sterilisation which may be used in the manufacture of Injections are described under *methods of sterilisation*, Appendix 6.2.

4. Containers : Containers for Injections are made from materials which are sufficiently transparent to permit the

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

visual inspection of the contents and which do not interact physically or chemically with the preparation in any manner likely to alter the strength, quantity or purity beyond the official requirements under the ordinary conditions of handling, shipment, storage, sale and use.

Containers are closed by fusion, or by application of suitable closures, in such manner as to prevent contamination or loss of contents. Containers may be ampoules, vials or bottles of glass or may be made of other suitable materials.

Single-dose containers are used for administration of the contents on one occasion only. They may be used for intrathecal, intracisternal, intracardial or intravenous injections and are to be preferred for all injections. They must be used for all injections administered at one time in volumes of 10 ml or more.

Multiple-dose containers permit the withdrawal of successive portions of the contents without removal or destruction of the closure and without changing the strength, quality or purity of the remaining portion. They may be used for intramuscular, subcutaneous or intracutaneous administration, but no multiple-dose container may contain a total volume of injection sufficient to permit the withdrawal of more than ten doses, unless otherwise stated in the individual monograph. The period of time between the withdrawal of the first and the final dose should not be unduly prolonged.

A multi-dose container for a sterile solid permits the addition of a suitable vehicle and withdrawal of portions of the resulting preparation in such a manner that the sterility of the product is maintained.

Containers of glass meet the requirements for Hydrolytic resistance stated under *Glass Container for Injectable Preparation*, Appendix 3.3.28 A, and containers of plastic and intended for packing products for parenteral use meet the requirements under *Plastic Containers*, Appendix 3.3.28B. Disposable transfusion and infusion assemblies of tubing comply with the requirements under *Transfusion and Infusion Assemblies*, Appendix 3.3.28 C.

5. Closures : Vials or bottles are fitted with suitable closures which ensure a good seal and prevent the access of contaminants. The plastic or rubber materials of which the closure is composed must be compatible with the preparation and be sufficiently firm and elastic to allow the passage of a needle with minimal shedding of particles and to ensure that the puncture is resealed when the needle is withdrawn.

Before use, closures should be washed with a suitable detergent and rinsed with and boiled in several changes of Purified Water. Closures made from rubber and synthetic materials are liable to absorb the ingredients of the injection with which they are used, e.g. the preservative. When an anti-microbial preservative is used the closure, when necessary, should be placed in a solution of that preservative in Purified Water containing at least twice the concentration to be used in the injection; the quantity of solution used should be sufficient to cover the closures and at least 2 ml for each g of material. The vessel should then be closed and heated at an appropriate combination of time and temperature. After heating, the closures should be kept in the sealed container until required for use.

When the injection with which the closures are to be used contains other added substances that are liable to be absorbed by the closure, these should be added to the solution in which the closures are to be heated in amounts equal to at least twice the concentration to be used in the injection.

Closures intended for containers of oily injectable preparations should be made of oil-resistant materials.

6. Inspection : Good Manufacturing Practice requires that each final container of Injection be subjected individually to a physical inspection, whenever the nature of the container permits, and that every container whose contents show evidence of contamination with visible foreign material be rejected.

Requirements of Tests

1. Appearance : Injections which are emulsions do not show any evidence of separation and show a uniform appearance after shaking. Injections which are suspensions may show a sediment which must be readily dispersible on shaking, and the suspension must remain sufficiently dispersed to enable the correct dose to be withdrawn from the container.

Where Injections consists of solid substances to be shaken with the prescribed volume of the appropriate liquid, the final product should be a clear and practically particle-free solution of a uniform suspension.

2. Particulate matter : Injections which are solutions, when examined under suitable conditions of visibility, are clear and practically free from particles that can be observed on visual inspection by the unaided eye.

Injections which are to be prepared by dissolving the contents of the sealed container in Water for Injection or as directed on the label yield solutions with no visible residue or undissolved matter.

3. Sterility: Injections comply with the *tests for sterility*, Appendix 4.6.

4. Pyrogens : All intravenous infusions comply with the *test for pyrogens*, Appendix 2.36, injecting 10 ml per kg of body weight into each animal unless otherwise stated in the individual monograph.

In the case of other injections, unless otherwise justified or authorised or stated in the individual monograph, when the volume to be injected in a single dose is 10 ml or more, the preparation complies with the *test for pyrogens*, Appendix 2.36.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

5. Extractable volume : (a) *For intravenous infusions*—Transfer the contents to a dry graduated cylinder. The measured volume is not less than the nominal volume.

(b) *For sterile solutions or suspensions*—Single-dose containers hold sufficient of the Injection to permit the withdrawal and administration of the nominal dose using the normal technique, but do not contain such an excess as to present a risk should the whole contents be administered.

Where the nominal volume does not exceed 5 ml, the containers comply with the requirements of Method 1 and where the nominal volume is greater than 5 ml, the containers comply with the requirements of Method 2. Suspensions should be shaken before the contents are withdrawn; oily injections may be warmed but should be cooled to 25° before measuring the volume.

Method 1—Use six containers, five for the test and one for rinsing the syringe used. Inspect the five containers to be used in the test visually; each contains approximately the same volume of the preparation.

Using a syringe with a capacity not exceeding twice the volume to be measured and fitted with a suitable needle, take up a small quantity of the liquid to be examined from the container reserved for rinsing the syringe, and discharge it from the syringe whilst the needle is pointing upwards so as to expel any air. Withdrawn as much as possible of the contents of one of the containers reserved for the test and transfer, without emptying the needle, to a dry graduated cylinder of such a capacity that the total combined volume to be measured occupies not less than 40 per cent of the nominal volume of the cylinder. Repeat the procedure until the contents of the five containers have been transferred; measure the volume. The average content of the five containers is not less than the nominal volume and not more than 115 per cent of the nominal volume.

Method 2—Transfer the contents of not less than three containers, separately, to dry graduated cylinders such that the volume to be measured occupies not less than 40 per cent of the nominal volume of the cylinder; measure the volume transferred. The content of each container is not less than the nominal volume and not more than 110 per cent of the nominal volume.

Multiple-dose containers labelled to yield a specific number of doses shall contain a sufficient excess to permit the withdrawal of the designated number of doses.

7. Uniformity of weight : Injections prepared by dissolving or reconstituting the contents of a sealed container before use comply with the requirements of the following test: Remove any adherent labels from a container and wash and dry the outside. Open the container and without delay weigh the container and its contents. Empty the container as completely as possible by gentle tapping, rinse if necessary with *water*, and then with *alcohol* and dry at 105° for one hour, or if the nature of the container precludes such treatment, dry at a lower temperature to constant weight. Allow to cool in a desiccator and weigh. The difference between the weights represents the weight of the contents. Repeat the procedure with a further nineteen containers, determine the average weight. Not more than two of the individual weights deviate from the average weight by more than 10 per cent and none deviates by more than 20 per cent.

8. Content of active ingredient : Where stated in the monograph, the following test is done on Injections prepared by dissolving or reconstituting the contents of a sealed container.

Determine the weight of the contents of ten containers as described under the test for **Uniformity of weight.** Mix the contents of the ten containers, carry out the Assay described in the monograph, and from the result calculate the proportionate amount of active ingredient in each container. Unless otherwise stated in the individual monograph, this amount does not deviate from the amount stated on the label by a greater percentage than that shown in Column A of the Table of Deviations except that in one container the amount may deviate by not more than the percentage shown in Column B.

TABLE OF DEVIATIONS

	Percentage Deviation	
Weight stated on lable	A	B
0.12 g or less	± 10 per cent	± 15 per cent
more than 0.12 g and less than 0.3 g	± 7.5 per cent	± 12.5 per cent
0.3 g or more	± 5 per cent	± 10 per cent

General Requirements

1. Packaging : The volume of any Injection in single-dose containers provides the amount specified for parenteral administration at one time and in no case is more than sufficient to permit the withdrawal and administration of one litre. Unless otherwise specified in the individual monograph, no multiple-dose container contains a volume of Injection more than sufficient to permit the withdrawal of 30 ml, and of more than ten doses.

2. Labelling : Containers of Injections are so labelled that a sufficient area of the container remains uncovered for its full length or circumference to permit inspection of the contents.

The label on the sealed container and on the package states (1) the name of the Injection; (2) in

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

the case of a liquid preparation, the percentage content by volume of drug or amount of drug in a specified volume; in the case of a drug preparation, the amount of active ingredient; (3) the route of administration; (4) the storage conditions; (5) the batch number; (6) the date of manufacture and date of expiry, if any; (7) the name and proportion of any added stabilising agent or preservative; (8) name and address of the manufacturer.

In the case of a drug preparation or other preparation to which a diluent is intended to be added before use, the label states (1) the amount of each active ingredient; (2) the composition of the recommended diluent; (3) the amount of diluent to be used to attain a specific concentration of active ingredient and the final volume of solution or suspension so obtained; (4) directions for storage of the constituted preparation; (5) the period within which the constituted preparation should be used and during which period it may be expected to have the required or labelled potency if it has been stored and directed.

Insulin Injection

Soluble Insulin

Category : Hypoglycaemic agent.

Dose : The dose is determined by the physician in accordance with the needs of the patient.

Usual strengths : 20 Units per ml; 40 Units per ml; 80 Units per ml.

Standards : Insulin Injection is a sterile solution of the specific anti-diabetic principle of the mammalian pancreas. It may be prepared by dissolving crystalline insulin having a potency of not less than 23 Units per mg, calculated with reference to the anhydrous material, in Water for Injection containing sufficient of a suitable substance such as Glycerin to render the preparation isotonic with blood, sufficient Hydrochloric Acid to adjust the pH to about 3.0 and sufficient of a suitable bactericide. The solution after sterilisation is assayed and the strength adjusted if necessary. It is distributed aseptically into sterile containers, which are then sealed so as to exclude micro-organisms.

It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated number of Units of insulin.

Description : Colourless or almost colourless liquid practically free from solid matter which deposits on standing.

pH : Between 2.5 and 3.5, Appendix 5.10.

Glycerin : Between 1.45 and 1.75 per cent w/v, determined by the following method : To 5 ml add 30 ml of *water*, a slight excess of a 10 per cent w/v solution of *sodium tungstate* and add slowly, with continuous stirring, 2 ml of *N sulphuric acid*. Filter, and wash the residue with *water*. Dilute the combined filtrate and washings to 200 ml with *water* and add 2 drops of *bromocresol purple solution* and *0.1N sodium hydroxide* until the solution just becomes blue. Add 0.7 g of *sodium periodate* and heat at 37° to 40° with occasional stirring for about fifteen minutes. Add 3 ml of *propylene glycol*, mix, allow to stand for three to five minutes, and titrate with *0.1N sodium hydroxide* until the blue colour just reappears. Each ml of *0.1N sodium hydroxide* is equivalent to 0.00921 g of glycerin.

Zinc : Not more than 40 µg per 100 Units of insulin, determined by the following method : Carry out the *determination of zinc*, Appendix 3.3.26, using an accurately measured volume equivalent to about 100 µg of Zinc.

Other requirements : Complies with the requirements stated under Injection.

Assay : Carry out the *biological assay of insulin, Method A* or *B*, Appendix 2.9, and express the results in Units per ml. The fiducial limits of error are not less than 80 per cent and not more than 125 per cent of the stated potency.

Storage : Store in multiple-dose containers at a temperature between 2° and 8°; it should not be allowed to freeze.

Labelling : The label on the container states (1) the number of Units per ml; (2) the animal source or sources of the insulin; (3) that the preparation should not be allowed to freeze; (4) the date after which the contents are not intended to be used; (6) the storage conditions.

Globin Zinc Insulin Injection

Globin Insulin

Category : Hypoglycaemic agent.

Dose : The dose is determined by the physician in accordance with the needs of the patient.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Usual strengths : 40 to 80 Units per ml.

Standards : Globin Zinc Insulin Injection is a sterile preparation of the specific antidiabetic principle of the mammalian pancreas in the form of a complex obtained by the addition of Globin and Zinc Chloride. It may be prepared from a sterile solution in suitably diluted Hydrochloric Acid of crystalline insulin having a potency of not less than 23 Units per mg, calculated with reference to the anhydrous material, by adding aseptically a solution of globin in the proportion of 3.6 to 4.0 mg for each 100 Units, a sufficient quantity of Zinc Chloride, of suitable substances such as glycerin to render the preparation isotonic with blood and of a suitable bactericide. The preparation is distributed aseptically into sterile containers, which are then sealed so as to exclude micro-organisms.

It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated number of Units of insulin.

Description : Almost colourless liquid, substantially free from turbidity and from matter which deposits on standing.

pH : Between 3.0 and 3.8, Appendix 5.10.

Glycerin : Complies with the test described under Insulin Injection.

Zinc : Not less than 0.25 mg and not more than 0.35 mg per 100 Units of Insulin, determined in the following manner:

Carry out the *determination of zinc*, Appendix 3.3.26, using an accurately measured volume equivalent to about 0.1 mg of zinc.

Other requirements : Complies with the requirements stated under Injections.

Assay : Carry out the *biological assay of insulin, Method A* or *B*, Appendix 2.9, and express the results in Units per ml. The fiducial limits of error are not less than 86 per cent and not more than 125 per cent of the stated potency.

Storage : Store in multiple-dose containers at a temperature between 2° and 8°; it should not be allowed to freeze.

Labelling : The label on the container states (1) the number of units per ml; (2) the animal source or sources of the insulin; (3) that the preparation should not be allowed to freeze; (4) the date after which the contents are not intended to be used; (5) the storage conditions.

Isophane Insulin Injection

Isophane Insulin; Isophane Protamine Insulin Injection; Isophane Insulin (NPH)

Category : Hypoglycaemic agent.

Dose : The dose is determined by the physician in accordance with the needs of the patient.

Usual strengths : 40 Units per ml; 80 Units per ml.

Standards : Isophane Insulin Injection is a sterile, buffered suspension of the specific antidiabetic principle of the mammalian pancreas in the form of a complex obtained by the addition of a suitable protamine. It may be prepared from crystalline insulin having a potency of not less than 23 Units per mg, calculated with reference to the anhydrous material. The amount of protamine corresponds to the isophane ratio and is not less than 0.3 mg and not more than 0.6 mg of protamine sulphate for each 100 Units of insulin. Isophane Insulin Injection contains Sodium Phosphate as a buffering agent, sufficient of a suitable substance to render the preparation isotonic with blood, a sufficient amount of a suitable bactericide, and not more than 0.04 mg of zinc for each 100 Units of insulin. The preparation is distributed aseptically in sterile containers which are then sealed so as to exclude micro-organisms.

It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated number of Units of insulin.

Description : White suspension, which on standing deposits a white sediment and leaves an almost colourless supernatant liquid. The sediment is readily resuspended on gentle shaking.

Particle size : When examined under a microscope, the particles in the sediment are seen as rod-shaped crystals, the majority having a dimension not less than 5 μm and rarely exceeding 60 μm. There are no large aggregates.

pH : Between 6.9 and 7.5, Appendix 5.10.

Zinc : Not more than 40 μg per 100 Units of insulin, determined by the following method : To an accurately measured volume of the well-shaken suspension equivalent to 100 μg of zinc, and 1 ml of *0.1N hydrochloric acid*, mix well and carry out the *determination of zinc*, Appendix 3.3.26.

Insulin in solution : Complies with the *test for insulin in solution*, Appendix 2.11.

Prolongation of insulin effect : Carry out the *test for prolongation of insulin effect*, Appendix 2.10. At the time when the mean blood-sugar level of the group

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

receiving the Standard Preparation is 100 per cent of its initial level, the mean blood-sugar level of the group receiving the preparation being tested shall be less than 100 per cent of its mean initial level. If the mean blood-sugar level of the group receiving the Standard Preparation does not return to 100 per cent of its initial level in six hours, make the comparison at the time when it has returned to 90 per cent of its initial level. At this time, the mean blood-sugar level of the group receiving the preparation being tested shall be less than 90 per cent of its initial level. If the mean blood-sugar level of the group receiving the Standard Preparation does not return to 90 per cent of its initial level in six hours, repeat the test.

Other requirements : Complies with the requirements stated under Injections.

Assay : Carry out the **Assay** described under Protamine Zinc Insulin Injection.

Storage : Store in multiple-dose containers at a temperature between 2° and 8°; it should not be allowed to freeze.

Labelling : The label on the container states (1) the number of Units per ml; (2) the animal source or sources of the insulin; (3) that the preparation should not be allowed to freeze; (4) that the container should be gently shaken before a dose is withdrawn; (5) the date after which the contents are not intended to be used; (6) the storage conditions.

Protamine Zinc Insulin Injection

Potamine Zinc Insulin

Category : Hypoglycaemic agent.

Dose : The dose is determined by the physician in accordance with the needs of the patient.

Usual strengths : 40 to 80 Units per ml.

Standards : Protamine Zinc Insulin Injection is a sterile buffered suspension of the specific antidiabetic principle of the mammalian pancreas in the form of a complex obtained by the addition of a suitable protamine and Zinc Chloride. It may be prepared by assaying a sterile solution of crystalline insulin having a potency not less than 23 Units per mg, adjusting its potency so that when diluted with the other constituents in sterile form, it contains the requisite number of Units per ml, and adding aseptically to it, a suitable protamine in the proportion of 1.0 to 1.7 mg of protamine sulphate for each 100 Units, a quantity of Zinc Chloride equivalent to 0.2 mg of zinc for each 100 Units, sufficient of a suitable substance to render the preparation isotonic with blood and sufficient of a suitable bactericide. The suspension is distributed aseptically into sterile containers. To each container is added sufficient of a sterile solution of Sodium Phosphate so that the final mixture contains 10 to 11 mg of Sodium Phosphate for every 100 Units and the pH is adjusted to about 7.2. The containers are then sealed so as to exclude micro-organisms.

It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated number of Units of insulin.

Description : White suspension which on standing deposits a white sediment and leaves an almost colourless supernatant liquid. The sediment is readily resuspended on gentle shaking.

pH : Between 6.9 and 7.5, Appendix 5.10.

Zinc : Not less than 0.20 mg and not more than 0.25 mg per 100 Units of Insulin, determined in the following manner: To an accurately measured volume of the well-shaken suspension equivalent to about 0.1 mg of zinc, add 1 ml of *0.1N hydrochloric acid*, mix well, and carry out the *determination of zinc*, Appendix 3.3.26.

Insulin in solution : Complies with the *test for insulin in solution*, Appendix 2.11.

Prolongation of insulin effect : Carry out the *test for prolongation of insulin effect*, Appendix 2.10. At the time when the mean blood-sugar level of the group receiving the Standard Preparation has returned to 100 per cent of its initial level, the mean blood-sugar level of the group receiving the preparation being tested shall not exceed 80 per cent of its mean initial level. If the mean blood-sugar level of the group receiving the Standard Preparation does not return to 100 per cent of its initial level in six hours, make the comparison at the time when it has returned to 90 per cent of its initial level. At this time, the mean blood-sugar level of the group receiving the preparation being tested shall not exceed 72 per cent of its initial level. If the mean blood-sugar of the group receiving the Standard Preparation does not return to 90 per cent of its initial level in six hours, repeat the test.

Other requirements : Complies with the requirements stated under Injections.

Assay : Add to the suspension 0.2 ml of *0.1N hydrochloric acid* per ml, allow to stand for an hour to ensure solution of the precipitate and carry out the *biological assay of insulin, Method A* or *B*, Appendix 2.9. The fiducial limits of error are not less than 80 per cent and not more than 125 per cent of the stated potency.

Storage : Store in multiple-dose containers at a temperature between 2° and 8°; it should not be allowed to freeze.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Labelling : The label on the container states (1) the number of Units per ml; (2) the animal source or sources of the insulin; (3) that the preparation should not be allowed to freeze; (4) that the container should be gently shaken before a dose is withdrawn; (5) the date after which the contents are not intended to be used; (6) the storage conditions.

Insulin Zinc Suspension

I.Z.S.; Insulin Zinc Suspension (mixed); Insulin Lente

Category : Hypoglycaemic agent.

Dose : The dose is determined by the physician in accordance with the needs of the patient.

Usual strengths : 40 Units per ml; 80 Units per ml.

Standards : Insulin Zinc Suspension is a sterile, buffered suspension of the specific antidiabetic principle of the mammalian pancreas in the form of a complex obtained by the addition of Zinc Chloride to insulin in a form insoluble in water. It may be prepared by mixing aseptically about 3 volumes of Insulin Zinc Suspension (Amorphous) and about 7 volumes of Insulin Zinc Suspension (Crystalline) and distributing the mixture aseptically into sterile containers, which are then sealed so as to exclude micro-organisms.

It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated number of Units of insulin.

Description : White suspension which on standing deposits a white sediment and leaves an almost colourless supernatant liquid. The sediment is readily resuspended on gentle shaking.

Particle size : When examined under a microscope, the majority of the particles in the suspension are seen as rhombohedral crystals, with a maximum dimension greater than 10 µm but rarely exceeding 40 µm; a considerable number of particle have no uniform shape and do not exceed 2 µm in maximum dimension.

pH : Between 6.9 and 7.5, Appendix 5.10.

Total zinc : Not more than 0.0095 per cent w/v (for preparation containing 40 Units of insulin per ml) and not more than 0.014 per cent w/v (for preparation containing 80 Units of insulin per ml), determined by the following method: To an accurately measured volume of the well-shaken suspension equivalent to about 0.1 mg of Zinc, add 1 ml of *0.1N hydrochloric acid*, mix well and carry out the *determination of zinc*, Appendix 3.3.26.

Zinc in solution : Not more than 70 per cent of the total zinc (for preparations containing 40 Units of insulin per ml) and not more than 55 per cent of the total Zinc (for preparations containing 80 Units of insulin per ml), determined as described in the test for **Total Zinc.**

Insulin extractable with buffered acetone solution : Between 27 and 40 per cent determined by the following method: Centrifuge a volume equivalent to 400 Units of insulin, calculated from the strength stated on the label, and reject the supernatant liquid. Suspend the residue in 3.3 ml of *water*, add 6.6 ml of *buffered acetone solution*, stir for three minutes, and again centrifuge. Transfer the supernatant liquid as completely as possible to a long-necked, round-bottomed flask, add 0.3 g of *nitrogen-free mercuric oxide*, 3 g of *anhydrous sodium sulphate*, and 6 ml of *nitrogen-free sulphuric acid*, heat over a low flame until the liquid is colourless, and boil for a further thirty minutes. Allow to cool, dilute carefully with *water*, add 1 g of *zinc powder*, shake and allow to stand for ten minutes. Add an excess of *sodium hydroxide solution*, immediately connect the flask to an ammonia distillation apparatus, mix the contents, and distil the liberated ammonia into 20 ml of *0.01N sulphuric acid* prepared with *carbon dioxide-free water*. Rinse the condenser tube into the flask containing the distillate, add sufficient *carbon dioxide-free water* to produce a total volume of about 50 ml, and titrate the excess of sulphuric acid with *0.01N sodium hydroxide* to pH 6.00, using a glass electrode. Centrifuge a further volume equivalent to 400 Units of insulin, calculated from the strength stated on the label, and reject the supernatant liquid. Dissolve the residue in 10 ml of a 5 per cent w/v solution of *nitrogen-free sulphuric acid*, transfer to a long-necked, round-bottomed flask, and complete the determination described above, beginning at the words "add 0.3 g of *nitrogen-free mercuric oxide* ...". Calculate the percentage of insulin extractable with buffered acetone solution from the formula 100 A/B, where A is the volume of *0.01N sulphuric acid* used in the first determination and B is the volume used in the second determination.

The result of the test is valid only if in carrying out the first determination omitting the insulin preparation, not more than 0.2 ml of *0.01N sulphuric acid* is required.

Insulin in solution : Complies with the test for *insulin in solution*, Appendix 2.11.

Prolongation of insulin effect : Complies with the test described under Isophane Insulin Injections.

Other requirements : Complies with the requirements stated under Injections.

Assay : Add to the suspension 0.2 ml of *0.1N hydrochloric acid* per ml, allow to stand for an hour to ensure solution of the precipitate and breakdown of the complex; carry out the *biological assay of insulin, Method A* or *B*, Appendix 2.9. The fiducial limits of error

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

are not less than 80 per cent and not more than 125 per cent of the stated potency.

Storage : Store in multiple-dose containers at a temperature between 2° and 8°; it should not be allowed to freeze.

Labelling : The label on the container states (1) the number of units per ml; (2) the animal source or sources of the insulin; (3) that the preparation should not be allowed to freeze; (4) that the container should be gently shaken before a dose is withdrawn; (5) the date after which the contents are not intended to be used; (6) the storage conditions.

Insulin Zinc Suspension (Amorphous)

Amorphous I.Z.S.; Prompt Insulin Zinc Suspension

Category : Hypoglycaemic agent.

Dose : The dose is determined by the physician in accordance with the needs of the patient.

Usual strengths : 40 Units per ml; 80 Units per ml.

Standards : Insulin Zinc Suspension (Amorphous) is a sterile, buffered suspension of the specific antidiabetic principle of the mammalian pancreas in the form of a complex obtained by the addition of Zinc Chloride to insulin in a manner such that the solid phase of the suspension is amorphous. It may be prepared by adding aseptically to crystalline insulin having a potency of not less than 23 Units per mg, calculated with reference to the anhydrous material, a suitable quantity of Zinc Chloride, an appropriate amount of a suitable substance to render the preparation isotonic with blood and a sufficient quantity of a suitable bactericide. The suspension is distributed aseptically into sterile containers which are then sealed so as to exclude micro-organisms.

It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated number of Units of insulin.

Description : White suspension which on standing deposits a white sediment and leaves an almost colourless supernatant liquid. The sediment is readily re-suspended on gentle shaking.

Particle size : When examined under a microscope, the particles in the suspension are seen to have no uniform shape and rarely exceed 2 μm in maximum dimension.

Other requirements : Complies with the requirements stated under Injections.

pH; Total zinc; Zinc in solution; Insulin in solution; Prolongation of insulin effect; Assay : Complies with the requirements stated under Insulin Zinc Suspension.

Storage : Store in multiple-dose containers at a temperature between 2° and 8°. it should not be allowed to freeze.

Labelling : The label on the container states (1) the number of Units per ml; (2) the animal source or sources of the insulin; (3) that the preparation should not be allowed to freeze; (4) that the containers should be gently shaken before a dose is withdrawn; (5) the date after which the contents are not intended to be used; (6) the storage conditions.

Insulin Zinc Suspension (Crystalline)

Crystalline I.Z.S.; Extended Insulin Zinc Suspension

Category : Hypoglycaemic agent.

Dose : The dose is determined by the physician in accordance with the needs of the patient.

Usual strengths : 40 Units per ml; 80 Units per ml.

Standards : Insulin Zinc Suspension (Crystalline) is a sterile, buffered suspension of the specific antidiabetic principle of ox pancreas in the form of a complex obtained by the addition of Zinc Chloride to insulin in the form of crystals insoluble in water. It may be prepared by adding to crystalline insulin having a potency of not less than 23 Units per mg, calculated with reference to the anhydrous material, a suitable quantity of Zinc Chloride, an appropriate amount of a suitable substance to render the preparation isotonic with blood and a sufficient quantity of a suitable bactericide. The solution is partially neutralised to allow crystallisation to occur and the pH of the crystalline suspension is adjusted to about 7.2. The suspension is distributed aseptically into sterile containers, which are then sealed so as to exclude micro-organisms.

Description : White suspension which on standing deposits a white sediment and leaves an almost colourless supernatant liquid. The sediment is readily resuspended on gently shaking.

Particle size : When examined under a microscope, the

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

particles in the suspension are seen to be rhombohedral crystals, the majority having a maximum dimension greater than 10 μm but rarely exceeding 40 μm.

Other requirements : Complies with the requirements stated under Injections.

pH; Total zinc; Zinc in solution; Insulin in solution; Prolongation of insulin effect; Assay : Complies with the requirements stated under Insulin Zinc Suspension.

Insulin extractable with buffered acetone solution : Not more than 15 per cent, determined by the method described under Insulin Zinc Suspension.

Storage : Store in multiple-dose containers at a temperature between 2° and 8°; it should not be allowed to freeze.

Labelling : The label on the container states (1) the number of Units per ml; (2) the animal source or sources of the insulin; (3) that the preparation should not be allowed to freeze; (4) that the container should be gently shaken before a dose is withdrawn; (5) the date after which the contents are not intended to be used; (6) the storage conditions.

Intraperitoneal Dialysis Fluid

Intraperitoneal Dialysis Solution; Peritoneal Dialysis Solution

Standards : Intraperitoneal Dialysis Fluid is a sterile solution of Magnesium Chloride, Calcium Chloride, Sodium Acetate, Sodium Chloride, Dextrose (Anhydrous) and Sodium Metabisulphite in Water for Injection. It contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of sodium, Na, not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of calcium, Ca, not less than 87.0 per cent and not more than 113.0 per cent of the stated amount of magnesium, Mg, not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of total chloride, Cl, not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of dextrose, $C_6H_{12}O_6$. It contains no antimicrobial agents.

Sodium Chloride	5.56 g
Sodium Acetate	4.76 g
Calcium Chloride	0.22 g
Magnesium Chloride	0.152 g
Sodium Metabisulphite	0.15 g
Dextrose (anhydrous)	17.0 g
Purified Water, sufficient to produce	1000 ml

Dissolve the ingredients, and mix. Filter the solution, place immediately in suitable containers and sterilise by heating in an autoclave; the type of autoclave used should be such that rapid cooling of the solution may be effected, in order to prevent caramelisation of the dextrose.

One litre contains approximately 130 mmol of Na^+, 1.5 mmol of Ca^{2+}, 0.75 mmol of Mg^{2+}, 100 mmol of Cl^- and 35 mmol of bicarbonate (as. acetate).

Description : Clear, almost colourless or pale-yellow liquid. Is dextro-rotatory.

Identification : (A) Complies with **Identification** test (A) described under Dextrose.

(B) It gives the reactions of *sodium*, of *calcium*, of *magnesium*, and of *chlorides*, Appendix 3.1.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using a volume of not less than 10 ml per kg of the rabbit's weight.

Sterility : Complies with the *tests for sterility*, Appendix 4.6.

Assay : (1) *For sodium* – Dilute appropriately with *water* and determine by Method A for *flame photometry*, Appendix 5.16 A, or by Method A for *atomic absorption spectrophotometry*, Appendix 5.16 B, measuring at 589 nm and using *sodium solution FP*, suitably diluted with *water*, for the standard solutions. Calculate the concentration of Na in mmol per litre.

(2) *For calcium* – To an accurately measured volume equivalent to about 0.1 mmol of calcium, add 40 ml of *water* and 10 ml of a 40 per cent w/v solution of *potassium hydroxide*, mix well, allow to stand for three minutes, and titrate with *0.02 M disodium ethylenediaminetetraacetate*, using *calcon mixture* as indicator. Each ml of *0.02 M disodium ethylenediaminetetraacetate* is equivalent to 0.02 mmol of Ca. Calculate the concentration of Ca in mmol per litre.

(3) *For magnesium* – To an accurately measured volume equivalent to 0.05 mmol of magnesium, add 40 ml of *water* and 20 ml of *ammonia buffer solution* and titrate with *0.02 M disodium ethylenediaminetetraacetate* using 50 mg of *mordant black 11 mixture* as indicator. Each ml of *0.02 M disodium ethylenediaminetetraacetate*, after a volume equivalent to the calcium present in the sample has been deduced, is equivalent to 0.02 mmol of Mg. Calculate the concentration of Mg in mmol per litre.

(4) *For total chloride* – To an accurately measured volume equivalent to about 2 mmol of chloride, add sufficient *water* to produce 50 ml and titrate with *0.1 N*

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

silver nitrate, determining the end-point potentiometrically. Each ml of *0.1N silver nitrate* is equivalent to 0.1 mmol of Cl.

(5) *For dextrose* – To a volume equivalent to about 1.2 g of dextrose, $C_6H_{12}O_6$, and 0.2 ml of *dilute ammonia solution* and sufficient *water* to produce 100 ml. Mix well and determine the *optical rotation* in a suitable polarimeter tube at 25°. Appendix 5.12. The observed rotation, in degrees, multiplied by 1.0425 A, where A is the ratio 2 divided by the length, in dm, of the polarimeter tube employed, represents the weight, in g, of dextrose, $C_6H_{12}O_6$, in the volume of the sample taken.

Storage : Store in single-dose containers of colourless, transparent glass or of suitable plastic material. Separation of solid particles from glass containers may occur on storage; solutions containing such particles must not be used.

Labelling : The label on the container states (1) the strength of the solution in terms of the number of millimoles (mmol) of each ion present per litre, the quantity of dextrose being expressed in terms of anhydrous, dextrose, $C_6H_{12}O_6$; (2) the volume of solution in the container; (3) that the solution is not for intravenous administration; (4) that any portion of the solution remaining after the contents are first used should be discarded; (5) that the preparation should not be used if it contains visible solid particles.

Iodine

I_2 Mol. Wt. 253.8

Category : Topical anti-infective.

Description : Heavy, bluish-black, brittle, rhombic prisms or plates with a metallic lustre; odour, characteristic; volatile at ordinary temperatures.

Solubility : Very slightly soluble in *water*; soluble in *alcohol*; freely soluble in *carbon disulphide* and in *chloroform*, in *solvent ether*, in *carbon tetrachloride* and in concentrated aqueous solutions of iodides.

Standards : Iodine contains not less than 99.5 per cent and not more than the equivalent of 100.5 per cent of I.

Identification : (A) When gently heated, it gives violet-coloured vapours which condense, forming a bluish-black crystalline sublimate.

(B) With a solution of *potassium iodide* and *starch*, a deep blue colour is produced which disappears on boiling but reappears on cooling.

Chloride and bromide : Triturate 3.5 g thoroughly with 35 ml of *water*, filter and decolorise the filtrate by the addition of a little *zinc powder*. To 25 ml of the filtrate so obtained, add 5 ml of *dilute ammonia solution*, and then 5 ml of *silver nitrate solution* added gradually, filter; dilute the filtrate to 50 ml, and acidify with 4 ml of *nitric acid*; the opalescence produced is not more than the standard opalescence in the *limit test for chloride*, Appendix 3.2.2.

Cyanides : To 5 ml of the filtrate obtained in the test for **Chloride and bromide** add a few drops of *ferrous sulphate solution* and 1 ml of *sodium hydroxide solution*, warm gently and acidify with hydrochloric acid, no blue or green colour is produced.

Non-volatile matter : Leaves not more than 0.1 per cent as residue when volatilised on a water-bath.

Assay : Weigh accurately about 0.5 g and dissolve in a solution of 1 g of *potassium iodide* in 5 ml of *water*. Dilute to 250 ml with *water*, add 1 ml of *dilute acetic acid*, and titrate with *0.1N sodium thiosulphate*, using *starch solution* as indicator. Each ml of *0.1N sodium thiosulphate* is equivalent to 0.01269 g of I.

Storage : Store in glass-stoppered bottles or in glass or earthern-ware containers with well-waxed bungs.

Iron and Ammonium Citrate

Ferric Ammonium Citrate

Category : Haematinic.

Dose : 1 to 3 g.

Description : Thin, transparent, dark red scales or granules or a brownish-red granular powder; odourless; taste, astringent. Deliquescent in moist air and is affected by light.

Solubility : Very soluble in *water*, almost insoluble in *alcohol*.

Standards : Iron and Ammonium Citrate is a complex ammonium ferric citrate. It contains not less than 20.5 per cent and not more than 22.5 per cent of Fe.

Identification : (A) Ignite gently and dissolve the residue in *hydrochloric acid*; the solution gives the reactions of *ferric salts*, Appendix 3.1.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

(B) Warm with *sodium hydroxide solution*; ammonia is evolved and the solution gives the reactions of *citrates*, Appendix 3.1.

Arsenic : Not more than 4 parts per million, Appendix 3.2.1.

Lead : Not more than 30 parts per million, determined by the following method : Dissolve 2g in 20 ml of *hydrochloric acid Sp.* and 8 ml of *water*, add 0.5 ml of *nitric acid Sp.* heat just to boiling, cool, transfer to a separator and extract with three quantities, each of 20 ml, of *solvent ether*; if the acid solution is still more than faintly yellow, extract with an additional 20 ml of *solvent ether*; reject the ether extracts. Transfer the acid solution to a narrow-necked flask, rinse the separator with 5 ml of *water*, and add the rinsings to the flask. Heat to remove dissolved ether, cool, make alkaline with *ammonia solution Sp.*, add 1 ml of *potassium cyanide solution Sp.*, dilute to 50 ml with *water* and add 0.1 ml of *sodium sulphide solution*. Any colour produced is not darker than that produced by mixing 10 ml of *hydrochloric acid Sp.*, 0.5 ml of *nitric acid Sp.* and 6 ml of *standard lead solution*, making alkaline with *ammonia solution Sp.* and adding 1 ml of *potassium cyanide solution Sp.* and 0.1 ml of *sodium sulphide solution*.

Zinc : Dissolve 2 g in a mixture of 20 ml of *hydrochloric acid* and 8 ml of *water*, add 0.5 ml of *nitric acid*, heat just to boiling cool and extract with three quantities, each of 20 ml, of *solvent ether*. If the acid solution is still more than faintly yellow, repeat the extraction with a fourth quantity of 20 ml, of *solvent ether*. Warm the acid solution on a water-bath to remove dissolved ether, cool and add sufficient *water* to produce 200 ml. To 10 ml add 1 g of *citric acid* and 0.1 g of *resorcinol*, neutralise with *dilute ammonia solution*, using *thymol blue solution* as indicator, and shake for one minute with two successive quantities, each of 20 ml, of *dithizone solution Sp.* To the combined extracts, add 10 ml of *0.1N hydrochloric acid*, shake for one minute, separate the acid layer and wash it with 2 ml of *chloroform*. To the acid layer add 3 ml of *N hydrochloric acid* and 20 ml of *ammonium chloride solution* and adjust the volume to 50 ml with *water*. Add 1 ml of *potassium ferrocyanide solution* and allow to stand for fifteen minutes. Any turbidity produced is not more than that produced by the addition of 1 ml of *potassium ferrocyanide solution* to a freshly prepared mixture of 4 ml of 0.011 per cent w/v solution of *zinc sulphate*, 4 ml of *N hydrochloric acid*, 20 ml of *ammonium chloride solution* and sufficient *water* to produce 50 ml.

Chloride : 0.2 g dissolved in 5 ml of *water* and boiled with 2 ml of *nitric acid* complies with the *limit test for chlorides*, Appendix 3.2.2.

Free ferric compound : A 1.0 per cent w/v solution gives no blue precipitate with *potassium ferrocyanide solution* unless acidified with *hydrochloric acid*.

Sulphate : 0.1 g dissolved in 5 ml of *water* and boiled with 2 ml of *hydrochloric acid* complies with the *limit test for sulphates*, Appendix 3.2.8.

Assay : Weigh accurately about 0.5 g, dissolve in a mixture of 15 ml of *water* and 1 ml of *sulphuric acid* and warm until the dark brown colour becomes yellow. After cooling the solution to 15° add, drop by drop *0.1N potassium permanganate* till a pink colour persisting for five seconds is obtained. Add 15 ml of *hydrochloric acid* and 2 g of *potassium iodide*, allow to stand for three minutes, add about 60 ml of *water* and titrate with *0.1N sodium thiosulphate* using *starch solution* as indicator. Each ml of *0.1N sodium thiosulphate* is equivalent to 0.005585 g of Fe.

Storage : Store in tightly-closed, light-resistant containers.

Iron Dextran Injection

Category : Haematinic.

Dose : By deep intramuscular injection, 1 to 2 ml daily.

Standards : Iron Dextran Injection is a sterile colloidal solution containing a complex of ferric hydroxide with dextrans of low molecular weight in Water for Injection. It contains not less than 4.75 per cent w/v and not more than 5.25 per cent w/v of iron, Fe.

Description : A dark brown solution.

Identification : (A) Add *dilute ammonia solution* to a few drops of the injection, previously diluted to 5 ml with *water*; no precipitate is produced.

(B) To 1 ml add 20 ml of *water* and 5 ml of *hydrochloric acid* and boil for five minutes. Cool, add an excess of *strong ammonia solution* and filter. Wash the precipitate with *water*, dissolve in the minimum volume of *dilute hydrochloric acid* and add sufficient *water* to produce 20 ml. The resulting solution gives the reactions of *ferric salts*, Appendix 3.1.

(C) Mix 1 ml with 100 ml of *water*; to 5 ml of this solution add 0.1 ml of *hydrochloric acid*, boil for thirty seconds, cool rapidly, add 2 ml of *strong ammonia solution* and 5 ml of *hydrogen sulphide solution*, boil to remove hydrogen sulphide, cool, and filter. Boil 5 ml of the filtrate with 5 ml of *potassium cupritartrate solution*; the solution remains greenish in colour and no precipitate is formed. Boil a further 5 ml of the filtrate with 0.5 ml of *hydrochloric acid* for five minutes, cool, add 2.5 ml of *sodium hydroxide solution* and 5 ml of *potassium cupritartrate solution* and again boil; a reddish precipitate is produced.

pH : Between 5.2 and 6.5, Appendix 5.10.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Content of dextrans : Between 17.0 and 23.0 per cent w/v, determined by the following method: Dilute 1.0 g to 500.0 ml with *water*, dilute 10.0 ml of this solution to 100.0 ml with *water*, transfer 3.0 ml of the second solution to a test-tube, and cool to 0°. Add to form a lower layer, 6.0 ml of a solution, prepared and maintained at 0°, containing 0.2 per cent w/v of *anthrone* in a mixture of 19 volumes of *sulphuric acid* and one volume of *water*, mix and immediately heat in a water-bath for five minutes. Cool and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 625 nm, Appendix 5.15 A. Repeat the operation using 3.0 ml of *water* in place of the dilution of the injection. From the difference between the *extinctions*, calculate the content of dextrose present from a reference curve prepared by treating suitable amounts of *dextrose* (*anhydrous*) by the same process. Each g of dextrose is equivalent to 0.94 g of dextrans. Determine the *weight per ml* of injection, Appendix 5.19 and calculate the percentage w/v of dextrans.

Non-volatile residue : Between 28.0 and 33.5 per cent w/v, determined by the following method: Transfer about 1 ml on 3 to 5 g of sand spread in a shallow layer in a stainless steel dish and weigh accurately, the dish and sand having been previously dried and weighed. Evaporate on a steam-bath to dryness, continue the drying in an oven at 105° for 15 hours, and weigh. Determine the *weight per ml* of the injection, Appendix 5.19 and calculate the percentage w/v of the non-volatile residue.

Absorption from injection site : Prepare a site over the semitendinosus muscle of one leg of each of two rabbits by clipping the fur and disinfecting the exposed skin. Inject each site with a dose of 0.4 ml per kg of body weight in the following manner. Place the needle in the distal end of the semitendinosus muscle at an angle such as to ensure that the full length of the needle is used, then pass it through the sartorius and vastus medialis muscles. House the rabbits separately. Seven days after the injection, sacrifice the rabbits and dissect the treated legs to examine the muscles; no heavy black deposit of unabsorbed iron compounds is observed, and the tissue is only lightly coloured.

Copper : To 5.75 g add 5 ml of *nitric acid* and heat until the vigorous evolution of brown fumes ceases. Cool, add 2 ml of *sulphuric acid* and heat again until fumes are evolved, adding *nitric acid* dropwise from time to time until oxidation is complete. Cool, add 25 ml of *hydrochloric acid*, warm to dissolve, cool and extract with four quantities, each of 25 ml, of *isobutyl acetate*, rejecting the extracts. Evaporate the acid solution to dryness, adding *nitric acid* dropwise if charring occurs. Dissolve the residue in 10 ml of *N hydrochloric acid*, reserving a portion of the solution for the test for **Zinc**.

To 1 ml add 25 ml of *water* and 1 g of copper-free *citric acid*, make alkaline to *litmus paper* with *dilute ammonia solution*, dilute to 50 ml with *water*, add 1 ml of *sodium diethyldithiocarbamate solution* and allow to stand for five minutes; any colour developed is not deeper than that produced when 3 ml of *dilute copper sulphate solution* and 1 ml of *N hydrochloric acid* is similarly treated.

Zinc : To 5 ml of the solution reserved in the test for **Copper** add 15 ml of *sodium hydroxide solution*, boil, filter, wash the residue with *water*, and dilute the combined filtrate and washings to 25 ml with *water*. To 5 ml add 5 ml of *4N hydrochloric acid* and 2 g *ammonium chloride*, dilute to 50 ml with *water*, add 1 ml of freshly prepared *potassium ferrocyanide solution* and allow to stand for twenty minutes. Any opalescence produced is not greater than that produced when 1 ml of freshly prepared *potassium ferrocyanide solution* is added to a solution prepared from 3 ml of *dilute zinc sulphate solution*, 3 ml of *N sodium hydroxide*, 6 ml of *N hydrochloric acid* and 2 g of *ammonium chloride* diluted to 50 ml with *water*, and allowed to stand for twenty minutes.

Chloride : To 5.0 ml add 75 ml of *water* and 0.05 ml of *nitric acid* and titrate immediately with *0.1N silver nitrate*, determining the end-point potentiometrically; not less than 6.8 ml and not more than 9.6 ml of *0.1N silver nitrate* is required.

Heavy metals : Not more than 20 parts per million, determined by the following method: To 16.0 ml of the solution prepared in the test for **Arsenic**, add 50 ml of *hydrochloric acid* and extract with four quantities, each of 20 ml, of *isobutyl acetate*, rejecting the extracts. Evaporate the acid solution to dryness and dissolve the residue in 20.0 ml of *water*. To 12.0 ml of the resulting solution add 1.2 ml of *thioacetamide reagent* and 2 ml of *acetate buffer, pH 3.5*, mix, and allow to stand for two minutes. Any brown colour produced is not more intense than that produced by similarly treating a mixture of 2.0 ml of *standard lead solution* and 2.0 ml of the solution being examined.

Arsenic : Not more than 2 parts per million, Appendix 3.2.1.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using not less than 0.5 ml per kg of the rabbit's weight, the rate of injection being 1 ml in fifteen seconds.

Undue toxicity : Inject 0.1 ml into a tail vein of each of ten mice, each weighing between 17 and 22 g; not more than three mice die within five days of injection. If more than three mice die within five days, repeat the test on another group of twenty mice. Not more than ten of the thirty mice used in the combined tests die within five days of injection.

Other requirements : Comply with the requirements stated under Injections.

Assay : To 2 g add 10 ml of *water* and 5 ml of *sulphuric acid* and stir for several minutes. Allow to stand for five minutes, cool, and dilute to 50 ml with *water*. Activate a suitable zinc amalgam 'reductor' by passing through the column 200 ml of a 5 per cent w/v solution of *sulphuric*

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

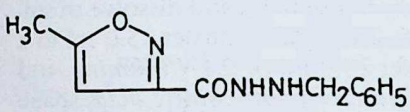
Digitized by Arya Samaj Foundation Chennai and eGangotri

acid pass the prepared solution slowly through the activated column, wash with 50 ml of *water*, four quantities, each of 25 ml, of a 5 per cent w/v solution of *sulphuric acid* and finally with 50 ml of *water*. Titrate the combined eluates with *0.1N ceric ammonium sulphate*, using *ferroin sulphate solution* as indicator. Each ml of *0.1N ceric ammonium sulphate* is equivalent to 0.005585 g of Fe. Determine the *weight per ml* of the injection, Appendix 5.19, and calculate the percentage w/v of Fe.

Storage : Store in single-dose or multiple-dose containers.

Labelling : The strength is stated as the equivalent amount of iron, Fe, in a suitable dose-volume.

Isocarboxazid



$C_{12}H_{13}N_3O_2$ Mol. Wt. 231.25

Category : Antidepressant.

Dose : Initial, upto 30 mg daily as a single dose or in divided doses; maintenance, 10 to 20 mg daily.

Description : White or creamy-white crystalline powder; odour, faint and characteristic; tasteless.

Solubility : Slightly soluble in *water*; soluble in *alcohol*; very soluble in *chloroform*.

Standards : Isocarboxazid is *N*-benzyl-*N'*-(5-methylisoxazole-3-ylcarbonyl) hydrazine. It contains not less than 98.0 per cent of $C_{12}H_{13}N_3O_2$, calculated with reference to the dried substance.

Identification : (A) Dissolve 10 mg in 10 ml of *acetone*, add 0.2 ml of *water* and 0.2 ml of a 1 per cent w/v solution of *ammonium molybdate* in *dilute hydrochloric acid*; an orange colour is produced.

(B) Dissolve 10 mg in 5 ml of *alcohol* and add 1 ml of a 1 per cent w/v solution of *dimethylaminobenzaldehyde* in *alcohol* containing 1 per cent v/v of *hydrochloric acid*; a yellow colour is produced.

Melting range : Between 105° and 108°, Appendix 5.11.

Chloride : Boil 0.5 g with 5 ml of *hydrogen peroxide solution (30 per cent)* and 10 ml of *sodium hydroxide solution* for two minutes. Cool, neutralise to *litmus* with *nitric acid* and add sufficient *water* to produce 40 ml; the resulting solution complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphated ash : Not more than 0.1 per cent, Appendix, 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying "in vacuo at 50°", Appendix 5.8.

Assay : Weigh accurately about 0.5 g and dissolve in 20 ml of *glacial acetic acid*. Add 20 ml of *hydrochloric acid* and 50 ml of *water*. Cool to about 15° and carry out the *nitrite titration*, Appendix 3.3.4. Each ml of *0.1M sodium nitrite* is equivalent to 0.02313 g of $C_{12}H_{13}N_3O_2$.

Storage : Store in well-closed containers.

Isocarboxazid Tablets

Category : Antidepressant.

Dose: Isocarboxazid. Initial dose, upto 30 mg daily, in divided doses; maintenance dose, 10 to 20 mg daily, in single or divided doses.

Usual strength : 10 mg.

Standards : Isocarboxazid Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Isocarboxazid, $C_{12}H_{13}N_3O_2$.

Identification : Extract a quantity of the powdered tablets equivalent to 10 mg of Isocarboxazid with *chloroform*, filter and evaporate the filtrate to dryness. The residue complies with **Identification** tests (A) and (B) described under Isocarboxazid.

Uniformity of content: Powder one tablet and dissolve as completely as possible in 35 ml of *acetone*. Add sufficient *acetone* to produce 50.0 ml and filter. On 1.0 ml of the filtrate carry out the **Assay**, beginning at the words "add 10.0 ml of *acetone*, 0.2 ml of *water*...". Calculate the content of $C_{12}H_{13}N_3O_2$ from the *extinction* obtained by carrying out the assay simultaneously on about 10 mg, accurately weighed, of *isocarboxazid R.S.* and from the declared content of $C_{12}H_{13}N_3O_2$ in the *isocarboxazid R.S.*

Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 90 and 110 per cent of the average except that for one tablet the content may be between 85 and 115 per cent of the average.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 20 mg of Isocarboxazid and dissolve as completely as possible in 70 ml of *acetone*. Add sufficient *acetone* to produce 100.0 ml and filter. To 1.0 ml of the filtrate add 10.0 ml of *acetone*, 0.2 ml of *water*, 0.2 ml of a 1 per cent w/v solution of *ammonium molybdate* in *dilute hydrochloric*

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

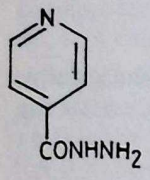
Digitized by Arya Samaj Foundation Chennai and eGangotri

acid, mix well, allow to stand for thirty minutes and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 420 nm, Appendix 5.15 A. Calculate the content of $C_{12}H_{13}N_3O_2$ from the *extinction* obtained by carrying out the Assay simultaneously on about 20 mg, accurately weighed, of *isocarboxazid R.S.* and from the declared content of $C_{12}H_{13}N_3O_2$ in the *isocarboxazid R.S.*

Storage: Store in well-closed, light-resistant containers.

Isoniazid

Isonicotinylhydrazide; I.N.H.



$C_6H_7N_3O$ Mol.Wt. 137.14

Category : Antibacterial (tuberculostatic).

Dose : 0.3 to 0.6 g daily, in divided doses.

Description : Colourless crystals or white or almost white, crystalline powder, odourless; taste, slightly sweet at first and then bitter.

Solubility : Freely soluble in *water*; sparingly soluble in *alcohol*, slightly soluble in *chloroform* and very slightly soluble in *solvent ether*.

Standards: Isoniazid is isonicotinylhydrazine. It contains not less than 98.0 per cent of $C_6H_7N_3O$, calculated with reference to the dried substance.

Identification: (A) Heat 50 mg with 1 g of *anhydrous sodium carbonate*; pyridine is evolved.

(B) Dissolve 0.1 g in 2 ml of *water* in a test-tube and add a hot solution of 0.1 g of *vanillin* in 10 ml of *water*. Allow it to stand and scratch the side of the test-tube with a glass rod; a yellow precipitate is obtained, which after isolation and re-crystallisation from 5 ml of *alcohol (70 per cent)*, has a melting range between 228° and 230°, Appendix 5.11.

(C) To a solution of 0.1 mg in 5 ml of *alcohol*, add 0.1 g of *borax* and 5 ml of a 5 per cent w/v solution of *1-chloro-2, 4-dinitrobenzene* in *alcohol*, evaporate to dryness on a water-bath and continue heating for a further ten minutes. To the residue add 10 ml of *methyl alcohol* and stir; a reddish-purple colour is produced.

(D) *Extinction* of a 1-cm layer of 0.001 per cent w/v solution in *0.01N hydrochloric acid* at 266 nm, about 0.43, Appendix 5.15 A.

Melting range : Between 170° and 175°, Appendix 5.11.

pH : Between 6.0 and 8.0, determined in a 5.0 per cent w/v solution, Appendix 5.10.

Heavy metals : Not more than 20 parts per million, determined by Method B on 1.0 g of substance, Appendix 3.2.4.

Hydrazine : To a solution of 2 mg in 2.0 ml of *water*, add 4.0 ml of *water* and 4.0 ml of a freshly prepared 0.2 per cent w/v solution of *dimethylaminobenzaldehyde* in a mixture of 6 volumes of *hydrochloric acid* and 4 volumes of *water* and allow to stand for three minutes. *Extinction* of a 1-cm layer of the resulting solution at 450 nm, using as the blank a mixture of 6.0 ml of *water* and 4.0 ml of the *dimethylaminobenzaldehyde solution* is not more than 0.05, Appendix 5.15 A.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, Appendix 5.8.

Assay : Weigh accurately about 0.4 g and dissolve in sufficient *water* to produce 250.0 ml. Transfer 25.0 ml to a glass-stoppered flask, add 25.0 ml of *0.1N bromine*, and cool to about 15°. Add 5 ml of *hydrochloric acid*, shake for one minute, and allow to stand for fifteen minutes in a water-bath maintained at about 15°. Add 10 ml of *potassium iodide solution* and titrate with *0.1N sodium thiosulphate*, using *starch solution* as indicator. Carry out a blank determination with the same quantities of the same reagents in the same manner but omitting the substance being examined. Each ml of *0.1N bromine* is equivalent to 0.003429 g of $C_6H_7N_3O$.

Storage : Store in well-closed, light-resistant containers.

Isoniazid Tablets

Isonicotinylhydrazide Tablets; I.N.H. Tablets

Category : Antibacterial (tuberculostatic).

Dose : Isoniazid, 100 to 300 mg daily, in single or divided doses.

Usual strengths : 50 mg; 100 mg; 300 mg.

Standards : Isoniazid Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Isoniazid, $C_6H_7N_3O$.

Identification : Shake a quantity of powdered tablets equivalent to 1 mg of Isoniazid with 50 ml of *alcohol* and filter; 5 ml of the filtrate complies with Identification test (C) described under Isoniazid.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

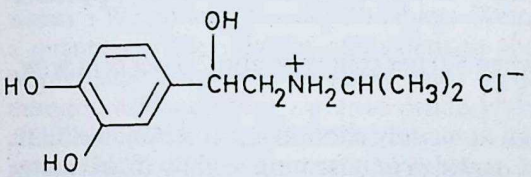
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of powder equivalent to about 0.4 g of Isoniazid and dissolve as completely as possible in *water*, filter and wash the residue with sufficient *water* to produce 250.0 ml. Transfer 25.0 ml of the solution to a glass-stoppered flask and carry out the **Assay** described under Isoniazid, commencing at the words "add 25.0 ml of *0.1N bromine*.....".

Storage: Store in well-closed, light-resistant containers.

Isoprenaline Hydrochloride

Isoproterenol Hydrochloride



$C_{11}H_{17}NO_3, HCl$ Mol. Wt. 247.72

Category : Adrenergic (bronchodilator).

Dose : By subcutaneous or intramuscular injection, 200 µg; by intravenous injection, 10 to 20 µg; 2 mg by intravenous infusion in Dextrose Injection according to the needs of the patient.

Description : White or almost white, crystalline powder; almost odourless; taste, slighly bitter. Darkens gradually on exposure to air and light.

Solubility : Freely soluble in *water*; sparingly soluble in *alcohol*; insoluble in *chloroform*, and in *solvent ether*.

Standards : Isoprenaline Hydrochloride is *N*-[2-hydroxy-2-(3,4-dihydroxyphenyl) ethyl]-isopropyl-ammonium chloride. It contains not less than 98.0 per cent and not more than the equivalent of 101.5 per cent of $C_{11}H_{17}NO_3$,HCl, calculated with reference to the dried substance.

Identification : (A) To 2 ml of a 1 per cent solution, add two drops of *ferric chloride test-solution*; an emerald-green colour develops, which, on gradual addition of *sodium bicarbonate solution* changes to blue and further to red.

(B) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

(C) The light absorption, in the range 240 to 350 nm, of a 1-cm layer of a 0.005 per cent w/v solution, exhibits a maximum only at 280 nm; *extinction* at 280 nm, about 0.5, Appendix 5.15 A.

Melting range : Between 165° and 170°, Appendix 5.11.

Sulphate : 0.3 g complies with the *limit test for sulphates*, Appendix 3.2.8.

Phenones : *Extinction* of a 1-cm layer of a 0.20 per cent w/v solution in *0.01N sulphuric acid* at 310 nm, not more than 0.5, Appendix 5.15 A.

Sulphated ash : Not more than 1.0 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.1 per cent, determined on 1.0 g by drying "in vacuo" for 4 hours, Appendix 5.8.

Assay : Weigh accurately about 0.5 g, dissolve in 50 ml of *glacial acetic acid*, add 10 ml of *mercuric acetate solution* and titrate with *0.1N perchloric acid* using *crystal-violet solution* as indicator. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02477 g of $C_{11}H_{17}NO_3, HCl$.

Storage : Store in tightly-closed, light-resistant containers.

Isoprenaline Hydrochloride Injection

Isoproterenol Hydrochloride Injection

Category : Adrenergic (bronchodilator).

Dose : Isoprenaline Hydrochloride. By subcutaneous or intramuscular injection, 200 µg; by intravenous injection, 10 to 20 µg; 2 mg by intravenous infusion in Dextrose Injection according to the needs of the patient.

Usual strength : 200 µg per ml.

Description : Colourless or very pale yellow liquid, gradually turning dark on exposure to light and air.

Standards : Isoprenaline Injection is a sterile solution of Isoprenaline Hydrochloride in Water for Injection containing suitable stabilisers. It contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of $C_{11}H_{17}NO_3, HCl$.

Identification : To 2 ml add two drops of *ferric chloride test-solution*; an emerald-green colour develops which on gradual addition of *sodium bicarbonate solution* changes to blue and then to red.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

pH : Between 2.5 and 3.5, Appendix 5.10.

Other requirements : Complies with the requirements stated under Injection.

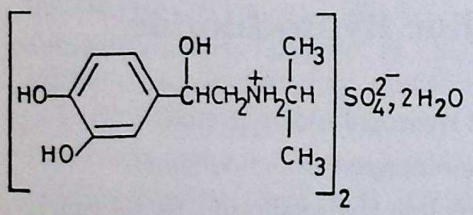
Assay : To a volume equivalent to 5 mg of Isoprenaline Hydrochloride add sufficient *water* to produce 50.0 ml. To 20.0 ml add 0.5 ml of *ferrous sulphate-citrate solution* and 2 ml of *glycine buffer solution*, mix and allow to stand for twenty minutes. Add sufficient *water* to produce 25.0 ml, mix and measure the *extinction* of a 1-cm layer of the resulting solution at 540 nm, Appendix 5.15 A. Calculate the content of $C_{11}H_{17}NO_3,HCl$ from the *extinction* obtained by repeating the determination using 5.0 ml of a 0.1 per cent w/v solution of *isoprenaline hydrochloride R.S.* instead of the injection and from the declared content of $C_{11}H_{17}NO_3,HCl$ in the *isoprenaline hydrochloride R.S.*

Storage : Store in single-dose, light-resistant containers at a temperature not exceeding 15°.

Labelling : The label on the container states (1) the storage conditions; (2) "Do not use the Injection if it is brown or contains a precipitate".

Isoprenaline Sulphate

Isoproterenol Sulphate



$(C_{11}H_{17}NO_3)_2,H_2SO_4,2H_2O$ Mol. Wt. 556.62

Category : Adrenergic (bronchodilator and cardiac stimulant).

Dose : 5 to 20 mg daily.

Description : White or almost white, crystalline powder; odourless; taste, somewhat bitter and astringent.

Solubility : Freely soluble in *water*; practically insoluble in *alcohol*, in *chloroform* and in *solvent ether*.

Standards : Isoprenaline Sulphate is the dihydrate of *N*-[2-hydroxy-2-(3, 4-dihydroxyphenyl) ethyl]-isopropylammonium sulphate. It contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of $(C_{11}H_{17}NO_3)_2,H_2SO_4$, calculated with reference to the anhydrous substance.

Identification : (A) Complies with **Identification** test (A) described under Isoprenaline Hydrochloride.

(B) To 5 ml of a 1.0 per cent w/v solution, add two drops of *silver nitrate solution*; a greyish precipitate is produced on standing, and the solution becomes pink.

(C) *Extinction* of a 1-cm layer of a 0.005 per cent w/v solution, at 279 nm, about 0.5, Appendix 5.15 A.

(D) A solution (1 in 20) gives the reactions of *sulphates*, Appendix 3.1.

(E) It melts at about 128°, with decomposition, Appendix 5.11.

pH : Between 4.0 and 5.5, determined in a freshly prepared 1.0 per cent w/v solution, Appendix 5.10.

Phenones : *Extinction* of a 1-cm layer of a 0.2 per cent w/v solution in *0.01N sulphuric acid* at 310 nm, not more than 0.2, Appendix 5.15 A.

Heavy metals : Not more than 10 parts per million, determined on 2.0 g by Method A, Appendix 3.2.4.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Water : Between 5.0 per cent w/w and 7.5 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately about 0.4 g and dissolve in 20 ml of *glacial acetic acid*, warming slightly if necessary. Cool and titrate with *0.1N perchloric acid* using *crystal-violet solution* as indicator. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.05206 g of $(C_{11}H_{17}NO_3)_2,H_2SO_4$.

Storage : Store in well-closed, light-resistant containers.

Isoprenaline Tablets

Isoprenaline Sulphate Tablets

Category : Adrenergic (bronchodilator and cardiac-stimulant).

Dose : Isoprenaline Sulphate, 5 to 20 mg daily.

Usual strength : 10 mg.

Standards : Isoprenaline Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Isoprenaline Sulphate, $(C_{11}H_{17}NO_3)_2,H_2SO_4,2H_2O$. The tablets may contain Citric Acid and Sodium Metabisulphite.

Identification : (A) Extract a quantity of the powdered tablets, equivalent to about 50 mg of Isoprenaline Sulphate, with 5 ml of *water* and filter. The filtrate complies with **Identification** tests (A) and (B) described under Isoprenaline Sulphate.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Uniformity of content : Crush one tablet and shake with 50 ml of *water* for fifteen minutes. Add sufficient *water* to produce 100.0 ml, mix and filter. To 20.0 ml of the filtrate add 0.5 ml of *ferrous sulphate-citrate solution* and 2 ml of *glycine buffer solution* and allow to stand for twenty minutes. Dilute to 25.0 ml with *water* and mix. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 540 nm, Appendix 5.15 A. Calculate the content of $(C_{11}H_{17}NO_3)_2, H_2SO_4, 2H_2O$, from the *extinction* obtained by repeating the determination using a suitable quantity of *isoprenaline sulphate R.S.* instead of the substance being examined and from the declared content of $(C_{11}H_{17}NO_3)_2, H_2SO_4, 2H_2O$ in the *isoprenaline sulphate R.S.*

Repeat the operation using a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 85 and 115 per cent of the average except that for one tablet the content may be between 80 and 120 per cent of the average.

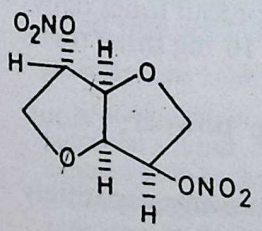
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.1 g of Isoprenaline Sulphate and shake with *water* for fifteen minutes. Add sufficient *water* to produce 100.0 ml, mix and filter. Dilute 20.0 ml of the filtrate to 200.0 ml with *water*. To 20.0 ml of the resulting solution, add 0.5 ml of *ferrous sulphate-citrate solution* and 2 ml of *glycine buffer solution*, allow to stand for twenty minutes, dilute to 25.0 ml with *water* and mix. Measure the *extinction* of a 1-cm layer of the resulting solution at 540 nm, Appendix 5.15 A. Calculate the content of $(C_{11}H_{17}NO_3)_2, H_2SO_4, 2H_2O$, from the *extinction* obtained by repeating the assay, using 0.1 g *isoprenaline sulphate R.S.* instead of the powder, and from the declared content of $(C_{11}H_{17}NO_3)_2, H_2SO_4, 2H_2O$ in the *isoprenaline sulphate R.S.*

Storage : Store in well-closed, light-resistant containers.

Diluted Isosorbide Dinitrate

Diluted Sorbide Nitrate



$C_6H_8N_2O_8$ Mol. Wt. 236.14

Category : Anti-anginal.

Dose : 20 to 300 mg of isosorbide dinitrate daily, in divided doses.

Description : Ivory-white, crystalline, powder; odourless.

Solubility : Very slightly soluble in *water*; sparingly soluble in *alcohol*; freely soluble in *chloroform*; very soluble in *acetone*.

Standards : Diluted Isosorbide Dinitrate is a dry mixture of 1,4:3,6-dianhydro-D-glucitol dinitrate with lactose or any other suitable inert excipient which permits safe handling. It contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of $C_6H_8N_2O_8$. It may contain upto 1.0 per cent of suitable stabilisers.

Identification : (A) To a quantity equivalent to about 50 mg of isosorbide dinitrate, in a sintered-glass crucible add 5 ml of *acetone* and collect the filtrate. Repeat with two further quantities, each of 5 ml, of *acetone* and evaporate the combined filtrate at a temperature not exceeding 35°, with the aid of a gentle current of air. Dry the residue "in vacuo" over *calcium chloride* at room temperature for sixteen hours. The *infra-red absorption spectrum* of a 2.5 per cent w/v solution of the residue in *chloroform* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of a similar preparation from the residue obtained from *diluted isosorbide dinitrate R.S.*, Appendix 5.15 B.

(B) Extract a quantity equivalent to 10 mg of isosorbide dinitrate with 10 ml of *solvent ether* and filter. Evaporate the filtrate to dryness at a temperature not exceeding 35°, and dissolve the residue in 0.15 ml of a 50 per cent v/v solution of *sulphuric acid* containing a trace of *diphenylamine;* an intense blue colour develops.

Heavy metals : Not more than 10 parts per million, determined on 2.0 g by Method B, Appendix 3.2.4.

Arsenic : Not more than 2 parts per million, Appendix 3.2.1.

Assay : Weigh accurately a quantity equivalent to about 25 mg of isosorbide dinitrate in a glass-stoppered flask and shake for fifteen minutes with 15 ml of *glacial acetic acid*. Add sufficient *glacial acetic acid* to produce 25.0 ml and filter. Pipette 1.0 ml of the filtrate into a 100-ml volumetric flask, add 2 ml of *phenoldisulphonic acid solution*, allow to stand for fifteen minutes, add 50 ml of *water*, make alkaline with *strong ammonia solution*, cool and dilute to volume with *water*. Measure the *extinction* of a 1-cm layer of the resulting solution at 405 nm, Appendix 5.15 A, using as the blank 1.0 ml of *glacial acetic acid* treated in a similar manner, beginning at the words "add 2 ml of *phenoldisulphonic acid solution*.....". Dissolve 0.2 g of *potassium nitrate*, previously dried at 105° in 5 ml of *water* and add sufficient *glacial acetic acid* to produce 25.0 ml. To 5.0 ml add sufficient *glacial acetic acid* to produce 50.0 ml. Using 1.0 ml of this solution

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

repeat the **Assay** beginning at the words "add 2 ml of *phenoldisulphonic acid solution*....". Calculate the content of $C_6H_8N_2O_8$ from the values of the extinctions so obtained. Each ml of the potassium nitrate solution is equivalent to 0.934 mg of $C_6H_8N_2O_8$.

Storage : Store in tightly-closed containers, in a cool place.

Labelling : The label on the container states the content of isosorbide dinitrate.

Isosorbide Dinitrate Tablets

Sorbide Nitrate Tablets

Category : Anti-anginal.

Dose : Isosorbide Dinitrate, 20 to 300 mg daily, in divided doses.

Usual strengths : 2.5 mg; 5 mg; 10 mg of isosorbide dinitrate.

Standards : Isosorbide Dinitrate Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Isosorbide Dinitrate, $C_6H_8N_2O_8$.

Identification : (A) Shake a quantity of the powdered tablets equivalent to 50 mg of Isosorbide Dinitrate with a warm 50 per cent v/v solution of *sulphuric acid* containing trace of *diphenylamine*; an intense blue colour develops.

(B) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and *toluene* as the mobile phase. Apply separately to the plate 20 µl of each of the following two solutions. For solution (1) extract a quantity of the powdered tablets equivalent to 2 mg of isosorbide dinitrate with 1 ml of *solvent ether* and centrifuge; for solution (2) dissolve 2 mg *isosorbide dinitrate R.S.* in 1 ml of *solvent ether*. After removal of the plate, dry it in a current of air, spray with a 1 per cent w/v solution of *diphenylamine* in *methyl alcohol* and irradiate for fifteen minutes with an ultra-violet lamp having wavelength maxima at 254 nm and 366 nm. The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

Disintegration : The *disintegration test for tablets* does not apply to tablets intended to be chewed before swallowing or allowed to dissolve in the mouth. Tablets intended to be swallowed intact comply with the *disintegration test for tablets*, Appendix 5.6.1.

Other requirements : Comply with the requirements stated under Tablets.

Uniformity of content : Crush one tablet, add 5.0 ml of *glacial acetic acid*, shake for one hour and centrifuge. Pipette 1 ml (in the case of 2.5 mg tablets) or a suitable volume of the supernatant liquid equivalent to 0.5 mg of isosorbide dinitrate, dilute to 1.0 ml with *glacial acetic acid*, if necessary, add 2 ml of *phenoldisulphonic acid solution*, allow to stand for fifteen minutes, add 25 ml of *water*, make alkaline with *strong ammonia solution*, cool and add sufficient *water* to produce 50.0 ml. Complete the **Assay** described under Diluted Isosorbide Dinitrate, beginning at the words "Measure the *extinction*.....". Calculate the content of $C_6H_8N_2O_8$ in the tablet.

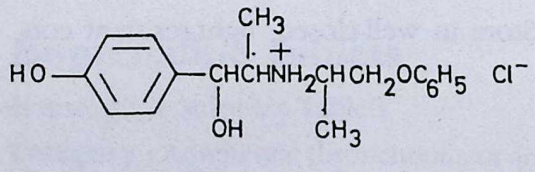
Repeat the operation using a further nine tablets. The content of each tablet is between 85 and 115 per cent of the average except that for one tablet the content may be between 80 and 120 per cent of the average.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 5 mg of Isosorbide Dinitrate, add 5.0 ml of *glacial acetic acid*, shake for one hour, centrifuge and carry out the **Assay** described under Diluted Isosorbide Dinitrate, beginning at the words "Pipette 1.0 ml.....".

Storage : Store in well-closed containers, in a cool place.

Labelling : The label on the container states (1) the strength in terms of the equivalent amount of isosorbide dinitrate; (2) whether the tablets are to be swallowed, chewed before swallowing or allowed to dissolve in the mouth.

Isoxsuprine Hydrochloride



$C_{18}H_{23}NO_3, HCl$ Mol. Wt. 337.85

Category : Peripheral vasodilator.

Dose : Oral, 10 to 20 mg, three or four times daily; by intramuscular injection, 5 to 10 mg three times daily.

Description : White, crystalline powder; odourless; taste, bitter.

Solubility : Slightly soluble in *water*; sparingly soluble in *alcohol*.

Standards : Isoxsuprine Hydrochloride is *N*- [(α-*SR*, 1*RS*)-1-(α, 4-dihydroxybenzyl)ethyl] ammo-

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

nium chloride. It contains not less than 97.0 per cent and not more than the equivalent of 103.0 per cent of $C_{18}H_{23}NO_3$, HCl, calculated with reference to the dried substance.

Identification : (A) To 1 ml of a 0.5 per cent w/v solution in *water* add 2 ml of *sodium nitrite solution* and 1 ml of *dilute sulphuric acid*. Add dropwise, *strong ammonia solution*; a yellow precipitate is produced which dissolves on the addition of *sodium hydroxide solution*.

(B) To 1 ml of a 0.5 per cent w/v solution in *water*, add 1 ml of *phosphomolybdic acid solution*; a pale yellow to white precipitate is produced.

(C) It melts at about 200° with decomposition, Appendix 5.11.

pH : Between 4.5 and 6.0, determined in a 1 per cent w/v solution in *water*, Appendix 5.10.

Heavy metals : Not more than 20 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

Sulphated ash : Not more than 0.5 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105° for one hour, Appendix 5.8.

Assay : Weigh accurately about 50 mg and dissolve, with the aid of heat, if necessary, in sufficient *water* to produce 1000.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 269 nm. Appendix 5.15 A. Calculate the content of $C_{18}H_{23}NO_3$, HCl, taking 71.5 as the value of E(1 per cent, 1-cm) at the maximum at about 269 nm.

Storage : Store in tightly-closed containers.

Ispaghula Husk

Isapgol Husk

Category : Laxative.

Dose : 3 to 5 g.

Standards : Ispaghula Husk consists of the epidermis and collapsed adjacent layers removed from the dried ripe seeds of *Plantago ovata* Forsk.

Description : Odourless; taste, bland and mucilaginous.

Macroscopical—Pale buff, brittle flakes, more or less lanceolate, upto 2 mm long and 1 mm wide at the centre, much broken into smaller fragments; many of the flakes having a small, brownish, oval spot, about 0.8 to 1.0 mm long, in the centre; the drug swells rapidly in water, forming a stiff mucilage.

Microscopical—Mounted in *cresol*, the particles are transparent and angular, the edges straight or curved and sometimes rolled. They are composed of polygonal cells with straight or slightly curved walls; the cells vary in size in different parts of the seed-coat. When mounted in *alcohol* and irrigated with *water*, the mucilage in the outer part of the epidermal cells swells rapidly and goes into solution, while the two inner layers of mucilage are more resistant and swell to form rounded papillae. When mounted in a 0.25 per cent w/v solution of *iodine*, occasional single and 2- to 4-compound starch granules, about 2 to 10 μm, can be seen in some of the cells. Occasional fragments of thick-walled, reddish-brown endosperm, and elongated fragments of grey embryo may be present.

Swelling power : 1 g, agitated gently and occasionally for four hours in a 25-ml stoppered cylinder filled to the 20-ml mark with *water* and allowed to stand for one hour, occupies a volume of not less than 20 ml and sets to a jelly.

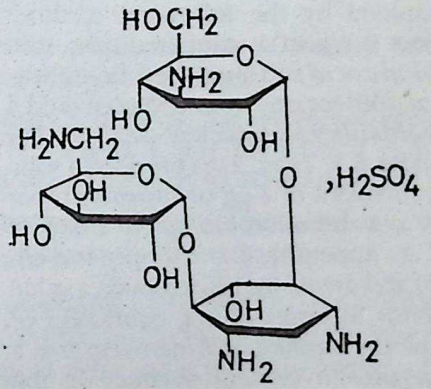
Ash : Not more than 4.5 per cent, Appendix 3.3.22.

Acid-insoluble ash : Not more than 0.45 per cent, Appendix 3.3.22.

Loss on drying : Not more than 12.0 per cent, determined on 1.0 g by drying in an oven at 105° for five hours, Appendix 5.8.

Storage : Store in well-closed containers, protected from moisture and against attack by insects and rodents.

Kanamycin Sulphate



$C_{18}H_{36}N_4O_{11}, H_2SO_4$ Mol. Wt. 582.58

Category : Antibacterial.

Dose : By intramuscular injection, the equivalent of 0.5 to 1 g (500,000 to 1,000,000 Units) of kanamycin base daily, in divided doses.

Description : White or almost white, crystalline powder; odourless or almost odourless.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Solubility : Freely soluble in *water*, practically insoluble in *acetone*; very slightly soluble in *chloroform* and in *solvent ether*.

Standards : Kanamycin Sulphate is the sulphate of 4-*O*-(6-amino-6-deoxy-α-D-glucopyranosyl)-6-*O*-(3-amino-3-deoxy-α-D-glucopyranosyl)-2-deoxy-D-streptamine, and antimicrobial base produced by *Streptomyces kanamyceticus* or by any other means. It has a potency not less than 750 Units per mg, calculated with reference to the dried substance.

Identification : (A) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel H* as the coating substance and a freshly prepared 3.85 per cent w/v solution of *ammonium acetate* as the mobile phase. Apply separately to the plate 1 µl of each of two solutions containing (1) 2 per cent w/v of the substance being examined and (2) 2 per cent w/v of *kanamycin sulphate R.S.* and, at a third point apply 1 µl of a mixture of equal volumes of solutions (1) and (2). After removal of the plate, allow it to dry in air for ten minutes. Then heat it at 105° for one hour, spray with a 0.1 per cent w/v solution of *ninhydrin* in *n-butyl alcohol* saturated with *water*, and heat at 105° for five minutes. The principal red spot in the chromatogram obtained with solution (1) corresponds with that in the chromatogram obtained with solution (2) and the principal red spot in the third chromato gram appears as a single compact spot.

Specific optical rotation : Between +112° and +123°, determined at 20° in a 5.0 per cent w/v solution, Appendix 5.12.

pH : Between 6.0 and 8.5, determined in a 1.0 per cent w/v solution, Appendix 5.10.

Kanamycin B : Not more than 5 per cent of the content of kanamycin, determined by the following method: Weigh accurately about 0.1 g in a stoppered tube, add 5.0 ml of *6N hydrochloric acid* and close the tube, tightly. Heat on a water-bath at 100° for one hour and cool. Add 4 ml of *6N sodium hydroxide* and sufficient sterile *buffer solution No.2*, Appendix 4.1, Table 2, to produce a solution containing the equivalent of 1 µg of kanamycin per ml (estimated). Carry out the *microbiological assay of antibiotics, Method A*, Appendix 4.1. Multiply the observed potency by 100 and divide by 126 to obtain a value representing the potency in terms of mg equivalent of Kanamycin B. Calculate the amount of Kanamycin B as a percentage of the Kanamycin content obtained in the **Assay.**

Sulphate : Between 15.7 and 17.3 per cent of SO_4, determined by the method described under Kanamycin Acid Sulphate.

Sulphated ash : Not more than 0.5 per cent, Appendix 3.2.7.

Loss on drying : Not more than 3.0 per cent, determined on 1.0 g by drying "in vacuo at 60°" for three hours, Appendix 5.8.

Assay : Carry out the *microbiological assay of antibiotics, Method A* or *B* and express the result in Units per mg, Appendix 4.1.

NOTE – 1.2 g of Kanamycin Sulphate is approximately equivalent to 1 g of kanamycin (1 million Units).

Kanamycin Sulphate intended for parenteral administration complies with the following additional requirements:

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using not less than 13 mg per kg of the rabbit's weight dissolved in not more than 5 ml of *water for injection*.

Histamine-like substances : Complies with the *test for histamine-like substances*, Appendix 2.35, using a solution containing 4 mg per ml in *water for injection*.

Sterility : Complies with the *tests for sterility*, Appendix 4.6.

Undue toxicity : Complies with the test described under Bacitracin, using 1.3 mg dissolved in 0.5 ml of *water for injection*.

Storage : Store in tightly-closed, light-resistant containers, in a cool place. If it is intended for parenteral administration, the container should be sterile and sealed so as to exclude micro-organisms.

Labelling : The label on the container states (1) the number of Units per mg or the equivalent weight of kanamycin base container in it; (2) the date after which the contents are not intended to be used; (3) the storage conditions; (4) whether or not the contents are intended for parenteral administration.

Kanamycin Acid Sulphate

Category : Antibacterial.

Dose : By intramuscular injection, the equivalent of 0.5 to 1 g (5,00,000 to 1,000,000 Units) of kanamycin base daily, in divided doses.

Description : White or almost white powder; odourless or almost odourless. Hygroscopic.

Solubility : Freely soluble in *water*, practically insoluble in *alcohol*; very slightly soluble in *chloroform* and in *solvent ether*.

Standards : Kanamycin Acid Sulphate is a form of kanamycin sulphate prepared by adding sulphuric acid to a solution of kanamycin sulphate and subsequently drying. It has a potency of not less than 650 Units per mg, calculated with reference to the dried substance.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Identification; pH; Kanamycin B; Sulphated ash : Complies with the tests described under Kanamycin Sulphate.

Specific optical rotation : Between +103° and +115°, determined at 20° in a 5.0 per cent w/v solution, Appendix 5.12.

Sulphate : Between 23.0 and 26.0 per cent of SO_4, calculated with reference to the dried substance and determined by the following method: Weigh accurately about 1 g, dissolve in 200 ml of *water*, add 3 ml of *hydrochloric acid*, heat to boiling and add 15 ml of hot *barium chloride solution*. Heat on a water-bath for four hours, collect the precipitate, wash with *water*, ignite and weigh. Each g of residue is equivalent to 0.4116 g of sulphate.

Loss on drying : Not more than 5.0 per cent, determined on 1.0 g by drying "in vacuo at 60°" for three hours, Appendix 5.8.

Assay : Carry out the *microbiological assay of antibiotics, Method A* or *B*, Appendix 4.1, and express the result in Units per mg.

Kanamycin Acid Sulphate intended for parenteral administration complies with the additional requirements for **Pyrogens, Histamine-like substances, Sterility** and **Undue toxicity** described under Kanamycin Sulphate.

Storage : Store in tightly-closed, light-resistant containers in a cool place. If it is intended for parenteral administration, the container should be sterile and sealed so as to exclude micro-organisms.

Labelling : The label on the container states (1) the number of Units per mg or the equivalent weight of kanamycin base contained in it; (2) the date after which the contents are not intended to be used; (3) the storage conditions; (4) whether or not the contents are intended for parenteral administration

Kanamycin Injection

Category : Antibacterial.

Dose : By intramuscular injection, the equivalent of 0.5 (500,000 Units) to 1 g (1,000,000 Units) of Kanamycin, in divided doses.

Usual strengths : The equivalent of 0.25 g (250,000 Units); 0.5 g (500,000 Units) of Kanamycin per ml or container.

Standards : Kanamycin Injection is either a sterile solution of Kanamycin Sulphate in Water for Injection, containing sulphuric acid and suitable buffering and stabilising agent or is prepared by dissolving the contents of a sealed container containing Kanamycin Acid Sulphate in the requisite amount of *water for injection* immediately before use.

Kanamycin Injection in the form of a sterile solution of Kanamycin Sulphate complies with the following requirements:

Content of Kanamycin : Not less than 97.0 per cent and not more than 110.0 per cent of the stated amount of kanamycin.

Description : Clear, colourless to pale yellow solution.

Identification : Complies with **Identification** test (A) described under Kanamycin Sulphate, preparing solution (1) by diluting the injection with *water* to contain 12.5 mg (12,500 Units) per ml.

pH : Between 4.0 and 6.0, Appendix 5.10.

Kanamycin B : Complies with the test described under Kanamycin Sulphate, using a volume equivalent to 0.1 g (100,000 Units) of Kanamycin.

Histamine-like substances : Complies with the test described under Streptomycin Sulphate, using a volume of the injection, diluted with *water* to contain the equivalent of 3 mg (3000 Units) per ml, corresponding to 1 ml per kg of the cat's weight.

Pyrogens : Complies with the test for pyrogens, Appendix 2.36, using a volume equivalent to not less than 10 mg (10,000 Units) per kg of the rabbit's weight diluted to not more than 5 ml with *water for injection*.

Undue toxicity : Complies with the test described under Bacitracin, the dose being 0.5 ml of a solution containing the equivalent of 1 mg (1000 Units) diluted with *water for injection*.

Other requirements : Complies with the requirements stated under Injections.

Assay : Carry out the *microbiological assay of antibiotics, Method A* or *B*, Appendix 4.1, and express the result in mg or Units of kanamycin per ml.

Storage : Store in single-dose or multiple-dose, light-resistant containers.

Labelling : The label on the container states (1) the strength in terms of the number of Units or the equivalent weight of kanamycin in a suitable dose volume; (2) the date after which the contents are not intended to be used; (3) the storage conditions.

Kanamycin Injection in the form of a sealed container containing Kanamycin Acid Sulphate complies with the following requirements:

Content of kanamycin : Determine the weight of the contents of each of ten containers as described in the test for **Uniformity of weight,** under Injections. Mix the

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

contents of the ten containers and carry out the *microbiological assay of antibiotics, Method A* or *B*, Appendix 4.1. From the result of the assay calculate the proportionate amount of kanamycin in each container. This amount is not less than 90.0 per cent and not more than 115.0 per cent of the amount stated on the label.

Other requirements : Complies with the requirements stated under Injections.

The contents of the sealed container, dissolved in the volume of *water for injection* stated on the label, comply with the requirements stated above for **Description, Identification, Kanamycin B, Histamine-like substances, Pyrogens** and **Undue toxicity** and with the following requirements.

pH : Between 6.5 and 7.5, Appendix 5.10.

Storage : Store in a cool, dry place. The constituted solution should be used within thirty minutes of preparation.

Labelling : The label on the sealed container states (1) the quantity of Kanamycin Acid Sulphate contained in it in terms of the number of Units or equivalent amount of kanamycin; (2) the volume of Water for Injection required for constituting the solution; (3) the date after which the contents are not intended to be used; (4) the storage conditions.

Heavy Kaolin

Category : Pharmaceutical aid.

Description : Soft, whitish or yellowish-white powder; odourless; taste, earthy or clay-like.

Solubility : Insoluble in *water*, in mineral acids and in solutions of alkali hydroxides.

Standards : Heavy Kaolin is a purified, natural hydrated aluminium silicate of variable composition.

Identification : Complies with the **Identification** test described under Bentonite.

Alkaline or Acid impurities : Shake 1.0 g for two minutes with 20 ml of freshly boiled and cooled *water* and filter. To 10 ml of the filtrate add two drops of *phenolphthalein solution*. The solution is colourless. Titrate with *0.01N sodium hydroxide* to a pink colour. Not more than 0.25 ml of *0.01N sodium hydroxide* is required.

Arsenic : Not more than 2 parts per million, Appendix 3.2.1.

Lead : To 1.0 g in a centrifuge tube add 5 ml of *dilute nitric acid* and digest for one hour in a boiling water-bath. Centrifuge until the solids are completely separated, and pour the supernatant liquid into a 100-ml volumetric flask. Add 5 ml of *dilute nitric acid* to the residue, mix well, and digest for fifteen minutes in a boiling water-bath. Centrifuge and add the supernatant liquid to the previous extract in the flask. Dilute to volume with *water*. On 50 ml of the resulting solution carry out the *limit test for lead*, Appendix 3.2.6, using 3 ml of *ammonium citrate solution Sp.*, 1 ml of *potassium cyanide solution Sp.* and 0.5 ml of *hydroxylamine hydrochloride solution Sp.*

Chloride : Boil 2 g with 40 ml of *water* and 10 ml of *dilute nitric acid* under a reflux condenser for five minutes, cool and filter. 50 ml of the filtrate complies with the *limit test for chlorides*, Appendix 3.2.2.

Adsorption power : In a glass-stoppered test-tube shake 1.0 g with 10 ml of a 0.37 per cent w/v solution of *methylene blue* for two minutes and allow to settle. Centrifuge and dilute the solution to one hunderd times its volume with *water*; the solution is not more intensely coloured than a solution of *methylene blue* containing 30 µg per ml.

Swelling power : Triturate 2 g with 2 ml of *water*; the mixture does not flow.

Iron : Triturate 2 g in a mortar with 10 ml of *water* and add 0.5 g of *sodium salicylate*; the mixture does not acquire more than a slight reddish tint.

Carbonate : Mix 1 g with 10 ml of *water* and 5 ml of *sulphuric acid*; no effervescence occurs.

Soluble matter : Not more than 1 per cent, determined by the following method: Boil 5.0 g with a mixture of 7.5 ml of *dilute hydrochloric acid* and 27.5 ml of *water* for five minutes, filter, wash the residue on the filter with *water* and dilute the combined filtrate and washings to 50.0 ml with *water*. To 10.0 ml of the solution add 1.5 ml of *dilute sulphuric acid*, evaporate to dryness on a water-bath, ignite and weigh.

Loss on ignition : Not more than 15.0 per cent, when ignited to constant weight at red heat.

Storage : Store in well-closed containers.

Light Kaolin

Category : Adsorbent (in the treatment of diarrhoea).

Dose : 15 to 75 g.

Description : Light, white powder free from gritty particles; odourless; almost tasteless; unctuous to the touch.

Solubility : Insoluble in *water* and in mineral acids.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Standards : Light Kaolin is a native hydrated aluminium silicate, freed from most of its impurities by elutriation and dried. It does not contain any dispersing agent.

Identification; Alkaline or Acid impurities; Arsenic; Lead; Chloride; Iron; Loss on ignition : Complies with the test described under Heavy Kaolin.

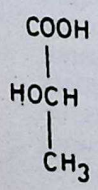
Loss on drying : 1.7 g, when dried to constant weight at 105°, loses not more than 1.5 per cent of its weight, Appendix 5.8.

Coarse Particles : Transfer 5.0 g to a stoppered cylinder about 35 mm in diameter and about 16 mm in length, add 60 ml of a 1 per cent w/v solution of *sodium pyrophosphate*, shake thoroughly, and allow to stand for five minutes. By means of a pipette, draw off 50 ml from a point about 5 cm below the surface of the liquid. To the liquid remaining add 50 ml of *water*, shake, allow to stand for five minutes, and draw off 50 ml in the same way as before. Repeat the operation until a total of 400 ml of suspension has been drawn off under the prescribed conditions. Transfer the remainder to an evaporating dish, and evaporate to dryness on a water-bath; the residue, after drying at 105°, weighs not more than 25 mg.

Fine particles : Disperse 5 g in 250 ml of *water* by shaking vigorously for two minutes in a stoppered flask, immediately pour into a glass cylinder 5 cm in diameter, and transfer 20-ml by means of a pipette to a glass dish; evaporate to dryness and dry at 105° to constant weight. Allow the remainder of the suspension to stand for four hours at 20° and withdraw a second 20-ml portion, using a pipette with its tip exactly 5 cm below the surface and without disturbing the sediment. Transfer the second portion to a glass dish, evaporate to dryness, and dry at 105° to constant weight. The weight of the residue from the second portion is not less than 70 per cent of the weight of the residue from the first portion.

Storage: Store in well-closed containers.

Lactic Acid



$C_3H_6O_3$ Mol. Wt. 90.08

Category : Pharmaceutical aid for Sodium Lactate Injection.

Description : Colourless or slightly yellow, syrupy liquid; nearly odourless; taste, sour; hygroscopic.

Solubility : Miscible in all proportions with *water*, with *alcohol* and with *solvent ether*. Practically insoluble in *chloroform*.

Standards : Lactic acid is a mixture of lactic acid, $C_3H_6O_3$, lactic anhydride $C_6H_{10}O_5$, lactoyl lactic acid and other polylactic acids and water. It contains the equivalent of not less than 85.0 per cent and more than 92.0 per cent w/w of $C_3H_6O_3$.

Identification : (A) Warm 1 g with 0.1 g of *potassium permanganate*; acetaldehyde is evolved.

(B) It gives the reactions of *lactates*, Appendix 3.1.

Wt. per ml : About 1.206 g, Appendix 5.19.

Arsenic : Not more than 1 part per million, Appendix 3.2.1.

Heavy metals : Not more than 10 parts per million, determined on 2.0 g by Method B, Appendix 3.2.4.

Iron : 1 g complies with the *limit test for iron*, Appendix 3.2.5.

Chloride : 1 g complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphate : 1 g complies with the *limit test for sulphates*, Appendix 3.2.8.

Citric, oxalic, phosphoric and tartaric acids : To 10 ml of a 10 per cent v/v solution add 40 ml of *calcium hydroxide solution* and boil for two minutes; no turbidity is produced.

Ether-isoluble substances : Dissolve 1.0 g in 25 ml of *solvent ether*; the solution is not more opalescent than 25 ml of *solvent ether*.

Volatile fatty acids : Heat cautiously 5 g in a glass-stoppered flask to a temperature of 50° to 60°; no unpleasant odour resembling that of the lower fatty acids is recognisable immediately after opening the flask.

Methyl alcohol and methyl esters : Not more than 0.05 per cent w/w, determined in the following manner: Place 2.0 g in a round-bottomed flask and add 10 ml of *water*. Cool in an ice-water mixture, cautiously add 30 ml of a 30 per cent w/v solution of *potassium hydroxide*, and cool in ice for a further ten to fifteen minutes. Steam distil the mixture into a 10-ml graduated cylinder containing 1 ml of *alcohol* collecting a volume of at least 9.5 ml and dilute to 10.0 ml with *water*. To 1.0 ml of the distillate add 5 ml of *potassium permanganate and phosphoric acid solution* and mix. After fifteen minutes add 2 ml of *oxalic acid and sulphuric acid solution*, stir with a glass rod until the solution is colourless, and then add 5 ml of *decolourised magenta solution*. After two hours any colour in the solution is not more intense than that of 1 ml of a reference solution containing 100 µg of *methyl alcohol* and 0.1 ml of *alcohol* treated in the same way beginning at the words "add 5 ml of *potassium permanganate and phosphoric acid solution*...".

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Reducing sugars : Dilute 1 g with 10 ml of *water*, neutralise with *sodium hydroxide solution*, add 5 ml of *potassium cupri-tartrate solution*, and boil, no red or greenish precipitate is formed.

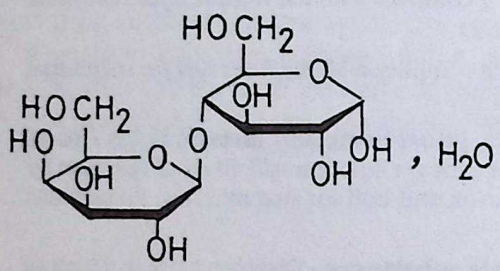
Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Assay : Weigh accurately about 0.2 g and dilute with 20 ml of *water*, add 50.0 ml of *0.1N sodium hydroxide*, stopper the flask, and allow to stand for thirty minutes. Titrate the excess of alkali with *0.1N hydrochloric acid* using *phenolphthalein solution* as indicator. Each ml of *0.1N sodium hydroxide* is equivalent to 0.009008 g of $C_3H_6O_3$.

Storage: Store in tightly-closed containers.

Lactose

Milk Sugar



$C_{12}H_{22}O_{11}, H_2O$ Mol. Wt. 360.31

Category : Pharmaceutical aid (tablet and capsule diluent).

Description : White or creamy-white crystalline powder; odourless; taste, slightly sweet.

Solubility : Freely soluble in *water*, and in boiling *water*; very slightly soluble in *alcohol*; practically insoluble in *chloroform* and in *solvent ether*.

Standards : Lactose is 4-*O*-*β*-galactopyranosyl-*α*-D-glucopyranose monohydrate.

Identification : (A) Add 5 ml of *N sodium hydroxide* to 5 ml of a saturated solution and gently warm the mixture; the liquid becomes yellow and finally brownish-red. Cool to room temperature, and add a few drops of *potassium cupri-tartrate solution* a red precipitate of cuprous oxide is formed.

(B) Heat 5 ml of a 5 per cent w/v solution with 5 ml of *strong ammonia solution* in a water-bath at 80° for ten minutes. A red colour develops.

Specific optical rotation : Between +54.8° and +55.5°, determined in a 10.0 per cent w/v solution prepared with addition of a few drops of *dilute ammonia solution*, Appendix 5.12.

Clarity, colour and odour of solution : A solution of 3 g in 10 ml of boiling *water* is clear, colourless and odourless.

Arsenic : Not more than 1 part per million, Appendix 3.2.1.

Heavy metals : Not more than 5 parts per million, determined by Method A on a solution prepared by dissolving 4.0 g in 20 ml of warm *water*, 1.0 ml of *0.1N hydrochloric acid* and sufficient *water* to produce 25 ml, Appendix 3.2.4.

Acidity : 5 g dissolved in 50 ml of freshly boiled *water*, requires for neutralisation not more than 0.5 ml of *0.1N sodium hydroxide*, using *phenolphthalein solution* as indicator.

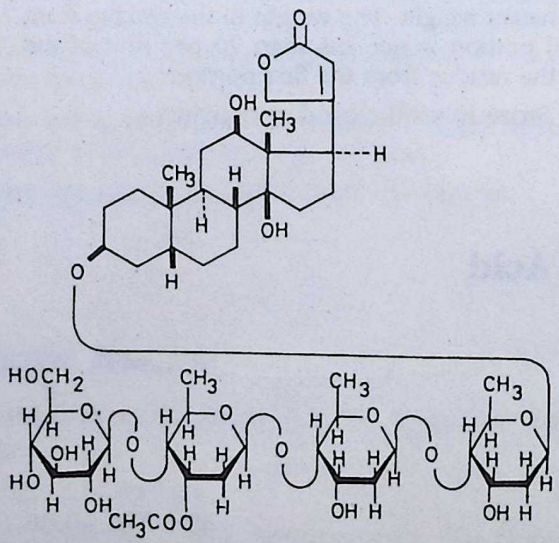
Alcohol-soluble matter : Shake 5 g of finely-powdered substance with 20 ml of *alcohol (90 per cent)* for ten minutes, filter, evaporate 10 ml of the filtrate to dryness and dry to constant weight at 105°; the residue does not weigh more than 12 mg.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Water : Not more than 5.5 per cent w/w, Appendix 3.3.25.

Storage : Store in well-closed containers.

Lanatoside C



$C_{49}H_{76}O_{20}$ Mol. Wt. 985.10

Category : Cardiotonic.

Dose : For rapid digitalisation, 1 to 1.5 mg in single

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

or divided doses. For maintenance, 0.25 to 0.75 mg daily.

Description : White, crystalline powder or colourless crystals; hygroscopic; odourless.

Solubility : Practically insoluble in *water*, and in *solvent ether*; slightly soluble in *chloroform.*

Standards : Lanatoside C is 3-[{*O*-*β*-D-glucopyranosyl-(1→4)-*O*-3-acetyl-2,6-dideoxy-*β*-D-*ribo*-hexopyranosyl-(1→4)-*O*-2, 6-dideoxy-*β*-D-*ribo*-hexopyranosyl-(1→4)-*O*-2, 6-dideoxy-*β*-D-*ribo*-hexopyranosyl}oxy]-12, 14-dihydroxy-3*β*, 5*β*, 12*β*, 14*β*-card-20(22)-enolide. It contains not less than 97.0 per cent and not more than the equivalent of 103.0 per cent of $C_{49}H_{76}O_{20}$, calculated with reference to the dried substance.

Identification : (A) Dissolve 5 mg in 5 ml of *glacial acetic acid*, add 0.1 ml of *ferric chloride test-solution* mix and add 2 ml of *sulphuric acid* slowly so as to form a lower layer; a brown ring is formed at the junction of the liquids and the upper layer develops a green colour which becomes blue on standing.

(B) Suspend 0.5 mg in 0.5 ml of *alcohol (60 per cent)* and add 0.25 ml of *dinitrobenzoic acid solution* and 0.1 ml of *dilute sodium hydroxide solution*; the suspension becomes violet.

(C) In the test for **Related substances** the principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

Specific optical rotation : Between +31.5° and +34.5°, determined at 20° in a 2 per cent w/v solution in *methyl alcohol*, Appendix 5.12.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3 using *kieselguhr G* as the coating substance. Place a dry plate in a tank containing a shallow layer of a mixture of 9 volumes of *acetone* and 1 volume of *formamide* and allow the solvent to ascend to the top. Remove the plate from the tank and allow the acetone to evaporate. Use the plate, with the flow of the mobile phase in the direction in which the equilibration was carried out, within two hours. Use a mixture of 50 volumes of *chloroform*, 6 volumes of *formamide*, and 50 volumes of *tetrahydrofuran*, as the mobile phase. Apply separately to the plate 2 µl of each of three solutions in a mixture of equal volumes of *chloroform* and *methyl alcohol* containing (1) 1.0 per cent w/v of the substance being tested; (2) 1.0 per cent w/v of *lanatoside C R.S.*; and (3) 0.1 per cent of the substance being tested. After removal of the plate, heat at 140° for fifteen minutes in a current of air, allow to cool, spray with a 10 per cent v/v solution of *sulphuric acid* in *alcohol* and heat at 140° for fifteen minutes. In the chromatogram obtained from solution (1) the intensity of any spots other than the principal spot is less than the intensity of the spots in the chromatogram obtained with solution (3).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 7.5 per cent, determined on 0.5 g by drying "in vacuo" for 24 hours, Appendix 5.8.

Assay : Weigh accurately about 0.03 g and dissolve in sufficient *methyl alcohol* to produce 50.0 ml. Dilute 25.0 ml to 100.0 ml with *methyl alcohol.* To 10.0 ml of the resulting solution add 6 ml of *alkaline picric acid solution* and dilute to 25.0 ml with *water.* Allow to stand for one hour and measure the *extinction* of a 1-cm layer of the solution at the maximum at about 490 nm, Appendix 5.15 A, using as the blank a mixture of 10.0 ml of *methyl alcohol* and 6 ml of *alkaline picric acid solution* diluted to 25.0 ml with *water.* The *extinction* is not less than 95.0 per cent and not more than 105.0 per cent of the *extinction* obtained by simultaneously carrying out the assay, using *lanatoside C R.S.* instead of the substance being tested, the quantities of both substances being calculated on the dried bases.

Storage: Store in well-closed, light-resistant containers.

Lanatoside C Tablets

Category : Cardiotonic.

Dose : Lanatoside C, initial 1.0 to 1.5 mg; maintenance dose, 0.25 to 0.5 mg.

Usual strength : 0.5 mg.

Standards : Lanatoside C Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Lanatoside C, $C_{49}H_{76}O_{20}$.

Identification : In the test for **Related substances** the principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

Uniformity of content : Powder one tablet, shake with 10.0 ml of *alcohol* for fifteen minutes and centrifuge, protecting the mixture from direct sunlight. On 5.0 ml of the clear supernatant liquid, carry out the **Assay** as directed below, beginning at the words "add 3.0 ml of *alkaline picric acid solution*....". Calculate the content of $C_{49}H_{76}O_{20}$ in the tablet.

Repeat the operation with a further nine tablets. The content of each tablet is between 90 per cent and 110 per cent of the average except that for one tablet the content may be between 85 per cent and 115 per cent of the average.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G*

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

as the coating substance and a mixture of 8 volumes of *hexane*, one volume of *solvent ether* and one volume of *glacial acetic acid* as the mobile phase and allowing the solvent to travel 13-cm beyond the line of application. Apply separately to the plate 2 µl of each of the following solutions: for solution (1) shake a quantity of the powdered tablets equivalent to 2.5 mg of Lanatoside C with 10 ml of a mixture of 10 volumes of *chloroform*, 5 volumes of *methyl alcohol* and 1 volume of *water*, filter, evaporate the filtrate to dryness and dissolve the residue in 5 ml of *methyl alcohol*; (2) a 0.05 per cent w/v of *lanatoside R.S.* in *methyl alcohol*; for solution (3) dilute 1 ml of solution (1) to 10 ml with *methyl alcohol*. After removal of the plate dry it in an oven at 100° for fifteen minutes, cool and develop once again with a mixture of 4 volumes of *n-propyl alcohol*, 1 volume of *ethyl acetate*, 4 volumes of *water* and 1 volume of *strong ammonia solution* as the mobile phase and allowing the solvent to travel 13 cm from the line of application. After removal of the plate dry it in an oven at 120° for one hour, cool and spray with a 5 per cent w/v solution of *potassium dichromate* in 40 per cent w/w solution of *sulphuric acid*. Any spot in the chromatogram obtained with solution (1) apart from the principal spot, is not more intense than the spot in the chromatogram obtained with solution (3).

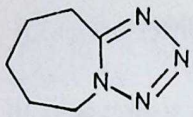
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 5 mg of Lanatoside C and shake with 50 ml of *alcohol* in a mechanical shaker for fifteen minutes, protecting the mixture from direct sunlight. Dilute to 100.0 ml with *alcohol*, mix and filter, discarding the first 20 ml of the filtrate.

To 5.0 ml of the filtrate add 3.0 ml of *alkaline picric acid solution* and mix by swirling. Allow to stand for twenty-five minutes, maintaining the temperature at 25 ± 3° and protecting the solution from direct light. Measure the *extinction* of a 1-cm layer of the solution at the maximum at about 490 nm, Appendix 5.15 A, using as the blank a mixture of 5.0 ml of *alcohol* and 3.0 ml of *alkaline picric acid solution*. Calculate the content of $C_{49}H_{76}O_{20}$ from the *extinction* obtained by simultaneously carrying out the **Assay** on 5.0 ml of a 0.005 per cent w/v solution of *lanatoside C R.S.* in *alcohol* and from the declared content of $C_{49}H_{76}O_{20}$ in the *lanatoside C R.S.*

Storage : Store in tightly-closed containers.

Leptazol



$C_6H_{10}N_4$ Mol. Wt. 138.17

Category : Central Nervous System stimulant.

Dose : 50 to 100 mg.

Description : Colourless crystals or white , crystalline powder; odourless; taste, slightly pungent, bitter.

Solubility : Readily soluble in *water*, in *alcohol*, in *chloroform* and in *solvent ether*.

Standards : Leptazol is 6,7,8,9-tetrahydro-5*H*-tetrazoazepine. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_6H_{10}N_4$, calculated with reference to the dried substance.

Identification : To a 10 per cent w/v solution add *mercuric chloride solution*; a white precipitate is obtained which, after recrystallisation from *water* or *alcohol*, melts at about 179°, Appendix 5.11.

Melting range : Between 57° and 60°, Appendix 5.11.

Acidity or Alkalinity : A 10 per cent w/v solution is neutral to *litmus solution*.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying "in vacuo" for twenty-four hours, Appendix 5.8.

Assay : Weigh accurately about 0.1 g, and dissolve in 25 ml of *water* in a stoppered flask. Add slowly with stirring, 25.0 ml of *cuprous chloride solution*. Stopper the flask and allow to stand for three hours with occasional shaking in a water-bath below 15°. Filter through a sintered-glass crucible and wash the flask and precipitate with 30 ml of *water* containing 1 per cent w/v solution of *glacial acetic acid*, the washing liquid being previously cooled to below 15°. To the mixed filtrate and washings, add 10 ml of *hydrogen peroxide solution* and if necessary, a few drops of *dilute sulphuric acid* to clarify the solution. After effervescence has ceased, heat gently to boil and continue boiling for ten minutes to decompose the excess of hydrogen peroxide. Cool to room temperature, add *dilute ammonia solution*, dropwise, to obtain an opalescence, and clear by the dropwise addition of *acetic acid*. Add 5 g of *potassium iodide*, titrate with *0.1N sodium thiosulphate* until the liquid is pale-brown. Add *starch solution*, and 3 g of *potassium thiocyanate*, and continue the titration until the colour is discharged. Repeat the operation

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

omitting the substance being examined, beginning at the words "add 10 ml of *hydrogen peroxide solution*". The difference between the titrations is equivalent to the amount of copper present in the precipitate. Each ml of *0.1N sodium thiosulphate* is equivalent to 0.007891 g of $C_6H_{10}N_4$.

Storage : Store in well-closed containers.

Leptazol Injection

Category : Central Nervous System Stimulant.

Dose : By subcutaneous injection, 0.5 to 1.0 ml.

Standards : Leptazol Injection is a solution of Leptazol in Water for Injection containing 0.25 per cent of Sodium Phosphate. It contains not less than 9.5 per cent and not more than 10.5 per cent w/v of $C_6H_{10}N_4$. It does not contain any added bacteriostatic agent.

Identification : To 5 ml add *mercuric chloride solution*, a white precipitate which after recrystallisation from *water* or *alcohol*, melts at about 179°, is formed, Appendix 5.11.

pH : Between 7.6 and 8.0, Appendix 5.10.

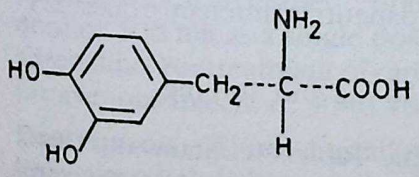
Other requirements : Complies with the requirements stated under Injections.

Assay : Dilute 1 ml with *water* to 25 ml and complete the **Assay** described under Leptazol, beginning at the words "Add slowly with stirring 25 ml *cuprous chloride solution*".

Storage : Store in single-dose containers.

Levodopa

L-Dopa



$C_9H_{11}NO_4$ Mol. Wt. 197.19

Category : Antiparkinsonian.

Dose : Initial, 250 mg daily, in divided doses, increasing gradually in accordance with the needs of the patient, maintenance dose, 2.5 to 8 g daily.

Description : White or almost white, crystalline powder; odourless; almost tasteless.

Solubility : Slightly soluble in *water*; freely soluble in aqueous solutions of mineral acids and alkali carbonates; practically insoluble in *alcohol*, in *chloroform* and in *solvent ether*.

Standards : Levodopa is 3-(3,4-dihydroxyphenyl)-L-alanine. It contains not less than 98.5 per cent and not more than the equivalent of 101.0 per cent of $C_9H_{11}NO_4$, calculated with reference to the dried substance.

Identification : (A) To 5 ml of a 0.1 per cent w/v solution in *0.1N hydrochloric acid* add 2 drops of *ferric chloride test-solution*; a green colour is produced. To half of the solution add an excess of *dilute ammonia solution*; a purple colour is produced. To the remainder of the solution add an excess of *sodium hydroxide solution*; a red colour is produced.

(B) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *microcrystalline cellulose* as the coating substance and a mixture of 50 volumes of *n-butyl alcohol*, 25 volumes of *glacial acetic acid* and 25 volumes of *water* as the mobile phase. Apply separately to the plate 5 µl of each of two solutions prepared immediately before use, in *N hydrochloric acid* containing (1) 1 per cent w/v of the substance being tested and (2) 1 per cent w/v of *levodopa R.S.* After removal of the plate, dry it in the current of warm air, and spray with a solution freshly prepared by mixing equal volumes of a 10 per cent w/v solution of *ferric chloride* and a 5 per cent w/v solution of *potassium ferricyanide*. The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

Clarity and colour of solution : Dissolve 2.0 g in sufficient *N hydrochloric acid* to produce 100.0 ml. The resultant solution is clear. 10 ml of this solution is not more intensely coloured than 10 ml of a mixture of 2.4 ml of *ferric chloride C.S.*, 0.6 ml of *cobalt chloride C.S.* and sufficient of a mixture of 1 volume of *dilute hydrochloric acid* and 9 volumes of *water* to make 200.0 ml.

Optical rotation : Between −1.27° and −1.34°, determined at 20° and using a solution prepared in the following manner: Dissolve a quantity equivalent to 0.20 g of the dried substance and 5 g of *hexamine* in 10 ml of *N hydrochloric acid*, add sufficient *N hydrochloric acid* to produce 25 ml and allow to stand in the dark for three hours, Appendix 5.12.

Light absorption : *Extinction* of a 1-cm layer of a 0.003 per cent w/v solution in *0.1N hydrochloric acid* at the maximum at about 280 nm, 0.41 to 0.43, Appendix 5.15 A.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *microcrystalline cellulose* as the coating substance and a mixture of 60 volumes of *isopropyl alcohol*, 15 volumes

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

of *ethyl methyl ketone* and 25 volumes of *N hydrochloric acid* as the mobile phase. Apply separately to the plate 5 µl of each of two solutions in *N hydrochloric acid* containing (1) 1.0 per cent w/v of the substance being tested and (2) 0.005 per cent w/v of the substance being tested. After removal of the plate, dry it in a stream of cold air for fifteen minutes and then at 100° for fifteen minutes. Allow to cool, spray with *cadmium and ninhydrin solution* and heat at 100° for thirty minutes. Any spot in the chromatogram obtained with solution (1), other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (2).

Heavy metals : Not more than 20 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.6 g and dissolve in 10 ml of *formic acid*, add 80 ml of *glacial acetic acid* and titrate with *0.1N perchloric acid*, using *oracet blue B solution* as indicator or alternatively determining the end-point potentiometrically, using a glass-calomel electrode system. Each ml of *0.1N perchloric acid* is equivalent to 0.01972 g of $C_9H_{11}NO_4$.

Storage : Store in well-closed, light-resistant containers, in a dry place.

Levodopa Capsules

L-Dopa Capsules

Category : Antiparkinsonian.

Dose : Levodopa. Initial dose, 250 mg daily, in divided doses, increasing gradually in accordance with the needs of the patient; maintenance dose, 2.5 to 8 g daily.

Usual strengths : 125 mg; 250 mg; 500 mg.

Standards : Levodopa Capsules contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Levodopa, $C_9H_{11}NO_4$.

Identification : (A) Shake a quantity of the contents of the capsules equivalent to 20 mg of Levodopa with 5 ml of *0.1N hydrochloric acid*. Add 2 drops of *ferric chloride test-solution*, a green colour is produced. To half of the solution add an excess of *dilute ammonia solution*; a purple colour is produced. To the remainder of the solution add an excess of *sodium hydroxide solution*; a red colour is produced.

(B) Comply with **Identification** test (B) described under Levodopa, using for solution (1) a solution obtained by shaking a quantity of the contents of the capsules equivalent to 0.1 g of Levodopa with 10 ml of *N hydrochloric acid* and filtering.

Related substances : Comply with the test described under Levodopa using as solution (1) a solution prepared by shaking a quantity of the contents of the capsules equivalent to 0.1 g of Levodopa with 10 ml of a mixture of equal volumes of *formic acid* and *methyl alcohol* prepared immediately before use.

Specific optical rotation : Between −38.5° and −41.5°, Appendix 5 12, determined in the following manner: Shake a quantity of the contents of the capsules equivalent to 0.50 g of Levodopa with 10 ml of *0.5N hydrochloric acid* for ten minutes and filter. Add 10 ml of a 21.5 per cent w/v solution of *sodium acetate*, and sufficient *water* to produce 50.0 ml, and measure the *optical rotation*. Calculate the *specific optical rotation* from the observed rotation and the content of Levodopa, $C_9H_{11}NO_4$, determined in the **Assay**.

Other requirements : Comply with the requirements stated under Capsules.

Assay : Weigh accurately a quantity of the mixed contents of 20 capsules equivalent to 0.6 g of Levodopa, dissolve in 10 ml of *formic acid*, add 80 ml of *glacial acetic acid* and titrate with *0.1N perchloric acid*, using *oracet blue B solution* as indicator. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.01972 g of $C_9H_{11}NO_4$.

Storage : Store in tightly-closed, light-resistant containers in a dry place.

Levodopa Tablets

L-Dopa Tablets

Category : Antiparkinsonian.

Dose : Levodopa. Initial dose, 250 mg daily, in divided doses, increasing gradually in accordance with the needs of the patient; maintenance dose, 2.5 to 8 g daily.

Usual strengths : 250 mg and 500 mg.

Standards : Levodopa Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Levodopa; $C_9H_{11}NO_4$.

Identification : (A) Shake a quantity of the powdered tablets equivalent to 20 mg of Levodopa with 5 ml of *0.1N hydrochloric acid*. Add 2 drops of *ferric chloride test-solution*; a green colour is produced. To half of the solution add an excess of *dilute ammonia solution*; a purple colour is produced. To the remainder of the

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

solution add an excess of *sodium hydroxide solution*; a red colour is produced.

(B) Comply with **Identification** test (B) described under Levodopa, using for solution (1) a solution obtained by shaking a quantity of the powdered tablets equivalent to 0.1 g of Levodopa with 10 ml of *N hydrochloric acid* and filtering.

Related substances : Comply with the test described under Levodopa using as solution (1) a solution prepared immediately before use by shaking a quantity of the powdered tablets equivalent to 0.1 g of Levodopa with 10 ml of a mixture of equal volume of *formic acid* and *methyl alcohol*.

Specific optical rotation : Comply with the test described under Levodopa Capsules, using a quantity of the powdered tablets equivalent to 0.50 g of Levodopa.

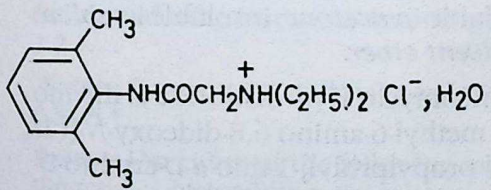
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 0.6 g of Levodopa and complete the **Assay** described under Levodopa Capsules, beginning at the words "dissolve in 10 ml of *formic acid*.....".

Storage : Store in tightly-closed, light-resistant containers in a dry place.

Lignocaine Hydrochloride

Lidocaine Hydrochloride



$C_{14}H_{22}N_2O, HCl, H_2O$ Mol. Wt. 288.82

Category : Local anaesthetic; cardiac depressant.

Dose : As local anaesthetic, upto 200 mg as a single dose or 500 mg as a single dose, when given with adrenaline. For treatment of cardiac arrhythmias, by intravenous injection, 50 to 100 mg.

Description : White, crystalline powder; odourless; taste, slightly bitter followed by a sensation of numbness.

Solubility : Very soluble in *water*; freely soluble in *alcohol*; soluble in *chloroform*; practically insoluble in *solvent ether*.

Standards : Lignocaine Hydrochloride is the monohydrate of *NN*-diethyl-(2,6-xylylcarbamoyl) methylammonium chloride. It contains not less than 99.0 per cent and not more than the equivalent of 100.5 per cent of $C_{14}H_{22}N_2O, HCl$ calculated with reference to the anhydrous substance.

Identification : (A) To 10 ml of a 2.5 per cent w/v solution, add *sodium hydroxide solution* till alkaline and filter. Wash the residue with *water* and dissolve 0.1 g of the residue in 1 ml of *alcohol*. Add 0.5 ml of a 10 per cent w/v solution of *cobalt chloride* and shake for two minutes; a bluish-green precipitate is produced.

(B) To 10 ml of a 1 per cent w/v solution, add 10 ml of *picric acid solution*, shake gently and allow the precipitate to crystallise; melting range of the precipitate after washing with *water*, and drying at 105°, between 227° and 231°, Appendix 5.11.

(C) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

Melting range : Between 74° and 79°, determined without previous drying, Appendix 5.11.

Clarity and colour of solution : Dissolve 1.0 g in 10 ml of *water*, the solution is clear and colourless.

pH : Between 4.0 and 5.5, determined in a 0.5 per cent w/v solution, Appendix 5.10.

Sulphate : Dissolve 0.2 g in 20 ml of *water*, add 2 ml of *3N hydrochloric acid*, mix, divide into two parts. To one part of the solution add 1 ml of *barium chloride solution*; no more turbidity is produced than is present in the remaining portion of the solution to which nothing has been added.

Heavy metals : Dissolve 0.2 g in 20 ml of *water*, add 2 ml of *3N hydrochloric acid*, mix and saturate the solution with *hydrogen sulphide*; no colour or precipitate results.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Water : Between 5.0 and 7.5 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately about 0.6 g, dissolve in 25 ml of *glacial acetic acid*, add 10 ml of *mercuric acetate solution* and titrate with *0.1N perchloric acid*, using *crystal-violet solution* as indicator. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02708 g of $C_{14}H_{22}N_2O,HCl$.

Storage : Store in well-closed containers.

Lignocaine and Adrenaline Injection

Lidocaine and Adrenaline Injection

Category : Local anaesthetic.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Dose : The dose should be determined by the prescriber.

CAUTION – It should never be given intravenously.

Usual strength : Lignocaine Hydrochloride, 20 mg and Adrenaline 0.01 mg per ml.

Standards : Lignocaine and Adrenaline Injection is sterile solution of Lignocaine Hydrochloride and Adrenaline Bitartrate in Water for Injection containing 0·1 per cent w/v of Sodium Metabisulphite. It contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Lignocaine Hydrochloride, $C_{14}H_{22}N_2O, HCl, H_2O$, and not less than 87.5 per cent and not more than 112.5 per cent of the stated amount of adrenaline, $C_9H_{13}NO_3$.

Description : Clear, colourless solution.

Identification : (A) To 5 ml add 1 ml of *hydrochloric acid*, cool to 0°, add 5 ml of 1 per cent *sodium nitrite solution* and pour the mixture into 2 ml of *β-naphthol solution* containing 1 g of *sodium acetate*, no red colour is produced.

(B) To 10 ml add 4 ml of *disodium hydrogen phosphate solution* and sufficient *0.1N iodine* to produce a distinct brown colour. Add *0.1N sodium thiosulphate* to remove the excess of *iodine*; a pink colour is produced.

(C) To 3 ml add 3 ml of *water* and 6 ml of *picric acid solution*, shake gently, and allow to stand till the precipitate becomes crystalline; melting range of precipitate after washing with *water* and drying at 105°, is between 227° and 231°, Appendix 5.11.

pH : Between 3.0 and 4.5, Appendix 5.10.

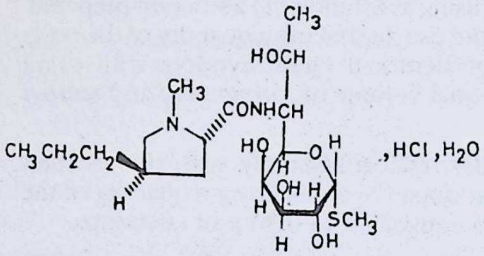
Assay : *For lignocaine hydrochloride* – Make a volume equivalent to 0.1 g of Lignocaine Hydrochloride, alkaline with *2N sodium hydroxide* and extract with three quantities, each of 20 ml of *chloroform*, washing each extract with the same 10 ml of *water*. Filter the washed extracts through a filter paper moistened with *chloroform*, wash the filter with 10 ml of *chloroform*, and titrate the combined filtrate and washings with *0.02N perchloric acid*, using *crystal violet solution* as indicator. Each ml of *0.02N perchloric acid* is equivalent to 0.005776 g of lignocaine hydrochloride, $C_{14}H_{22}N_2O, HCl, H_2O$.

For adrenaline – To a volume equivalent to 0.2 g of Lignocaine Hydrochloride add 20 mg of *sodium pyrosulphite*, 0.1 ml of *ferrous sulphate-citrate solution*, add 1 ml of *glycine buffer solution*. Mix, allow to stand for ten minutes, extract with 10 ml of *solvent ether*, allow to separate, reject the ether, and measure the *extinction* of a 4-cm layer at 540 nm, Appendix 5.15 A. Calculate the content of adrenaline, $C_9H_{13}NO_3$, from a reference curve prepared by treating suitable aliquots of a solution of *adrenaline bitartrate* by the same process.

Storage : Store in single-dose, light-resistant containers.

Labelling : The label on the container states (1) the percentage w/v of Lignocaine Hydrochloride; (2) the proportion of adrenaline base.

Lincomycin Hydrochloride



$C_{18}H_{34}N_2O_6S, HCl, H_2O$ Mol. Wt. 461.01

Category : Antibacterial.

Dose : The equivalent of 1.5 g of lincomycin daily, in divided doses, thirty minutes before food.

By intramuscular injection, the equivalent of 0.6 to 1.2 g of lincomycin daily, in two doses.

By intravenous infusion, the equivalent of 600 mg of lincomycin every eight hours.

Description : White or almost white, crystalline powder; odour slight and characteristic; taste, bitter.

Solubility : Freely soluble in *water*; soluble in *dimethyl formamide*; sparingly soluble in *alcohol*; very slightly soluble in *acetone*; insoluble in *chloroform* and in *solvent ether*.

Standards : Lincomycin Hydrochloride is the monohydrate of methyl-6-amino-6,8-dideoxy-*N*-[(2*S*, 4*R*)-1-methyl-4-propylprolyl]-1-thio-α-D-erythro-D-galacto-octopyranoside hydrochloride, an antimicrobial substance produced by *Streptomyces lincolnensis* var. *lincolnensis* or by any other means. It contains an amount of $C_{18}H_{34}N_2O_6S$ equivalent to the antibiotic activity of not less than 790 mcg of lincomycin per mg, calculated with reference to the anhydrous substance.

Identification : (A) The infra-red absorption spectrum exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *lincomycin hydrochloride R.S.*, Appendix 5.15 B.

(B) A 1 per cent w/v solution gives the reactions of *chlorides*, Appendix 3.1.

Specific optical rotation : Between +135° and +150°, determined in a 4 per cent w/v solution, Appendix 5.12.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

pH : Between 3.0 and 5.5, determined in a 10 per cent w/v solution, Appendix 5.10.

Lincomycin B : Carry out the method for *gas-liquid chromatography*, Appendix 5.4.1, using the following solutions: (1) dissolve 50 mg of *tetraphenylcyclopentadienone R.S.* (internal standard) and 50 mg of *lincomycin hydrochloride R.S.* in 5 ml of *pyridine* warming for five minutes if necessary to effect solution; to the cooled solution add 1 ml of *hexamethyldisilazane* and 0.5 ml of *trimethylchlorosilane*, allow to stand for thirty minutes, centrifuge for fifteen minutes and use the supernatant liquid; (2) treat 50 mg of the substance being examined in 5 ml of *pyridine* in a similar manner; (3) treat 50 mg of the substance being examined and 50 mg of the internal standard in 5 ml of *pyridine* in a similar manner. Carry out the chromatographic procedure using (a) a glass column 1.5 m long and 0.3 cm in internal diameter packed with 3 per cent w/w of silicone gum rubber (methyl) such as SE-30 supported on silanised diatomaceous earth (such as Gas-chrom Q, 100-120 mesh), maintained at 260°, (b) nitrogen as the carrier gas, and (c) a flame ionisation detector maintained at a temperature between 260° and 290°. The elution order is lincomycin B, lincomycin and the internal standard. If necessary, adjust the current setting for the lincomycin B peak to give a satisfactory response relative to that of the lincomycin peak. The area of the peak due to the trimethylchlorosilane derivative of lincomycin B, when corrected for the sensitivity factor, is not more than 5 per cent of the area of the peak due to the trimethylchlorosilane derivative of lincomycin.

Undue toxicity : Complies with the test described under Bacitracin, using 2.5 mg dissolved in 0.5 ml of *saline solution.*

Sulphated ash : Not more than 0.5 per cent, Appendix 3.2.7.

Water : Between 3.0 and 6.0 per cent w/w, Appendix 3.3.25.

Assay : Use either of the following methods; however, the results obtained from the microbiological assay shall be official.

(1) Carry out the method for *gas-liquid chromatography* described under the test for **Lincomycin B**. Calculate the content of $C_{18}H_{34}N_2O_6S$, from the declared content of $C_{18}H_{34}N_2O_6S$ in *lincomycin hydrochloride R.S.*

(2) Carry out the *microbiological assay of antibiotics, Method A*, Appendix 4.1, and express the result in µg of lincomycin per mg.

Lincomycin Hydrochloride intended for parenteral administration complies with the following additional requirements:

Histamine-like substances : Complies with the *test for histamine-like substances*, Appendix 2.35, using a solution containing 3.5 mg per ml.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using not less than 0.6 mg per kg of the rabbit's weight dissolved in not more than 5 ml of *saline solution.*

Sterility : Complies with the *tests for sterility*, Appendix 4.6.

Storage : Store in well-closed containers in a cool place. If it is intended for parenteral administration, the container should be sterile and sealed so as to exclude micro-organisms.

Labelling : The label on the container states (1) the date after which the contents are not intended to be used; (2) the storage conditions; (3) whether or not the contents are intended for parenteral administration.

Lincomycin Capsules

Category : Antibacterial.

Dose : The equivalent of 1.5 g of lincomycin daily, in divided doses, thirty minutes before food.

Usual strength : 500 mg.

Standards : Lincomycin Capsules contain a quantity of Lincomycin Hydrochloride equivalent to not less than 90.0 per cent and not more than 120.0 per cent of the stated amount of Lincomycin, $C_{18}H_{34}N_2O_6S$.

Identification : In the **Assay** the retention time of the principal peak due to Lincomycin Hydrochloride relative to that of the internal standard in solution (3) is the same as the retention time of the principal peak due to *lincomycin hydrochloride R.S.* relative to that of the internal standard in solution (1).

Lincomycin B : On an accurately weighed quantity of the mixed contents of 20 capsules, carry out the method for **Lincomycin B** described under Lincomycin Hydrochloride. The area of the peak due to the trimethylchlorosilane derivative of lincomycin B, when corrected for the sensitivity factor is not more than 5 per cent of the area of the peak due to the trimethylchlorosilane derivative of lincomycin.

Water : Not more than 7.0 per cent w/w, determined on the contents of the capsules, Appendix 3.3.25.

Other requirements : Comply with the requirements stated under Capsules.

Assay : Use either of the following methods; however the results obtained from the microbiological assay shall be official.

(1) On the mixed contents of 20 capsules, carry out the method for *gas-liquid chromatography* described under the test for **Lincomycin B**. Calculate the content of

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

$C_{18}H_{34}N_2O_6S$ from the declared content of $C_{18}H_{34}N_2O_6S$ in *lincomycin hydrochloride R.S.* and express the result in mg of lincomycin per capsule.

(2) On the mixed contents of 20 capsules, carry out the *microbiological assay of antibiotics, Method A*, Appendix 4.1, and express the result in mg of lincomycin per capsule of average weight.

Storage : Store in well-closed containers, at a temperature not exceeding 30°.

Labelling : The label on the container states (1) the strength in terms of the equivalent amount of lincomycin; (2) the date after which the capsules are not intended to be used; (3) the storage conditions.

Absorbent Lint

Lint; Cotton Lint; Unmedicated Lint

Category : Surgical dressing.

Description : Cotton cloth of plain weave, reasonably free from weaving defects, readily tearable in both directions and bleached to a good white having on one side a nap raised from either the warp or weft yarns and reasonably free from naps; it is clean and reasonably free from leaf, shell and other foreign substances.

Standards : Absorbent Lint is a cotton cloth of plain weave, on one side of which a nap has been raised from either warp or weft yarns. It absorbs water readily but its absorbency may be considerably reduced by medication, the absorbency of the product depending upon the medicament incorporated. It has not less than 98 per cent of the dimensions stated on the label.

Yarn : Reasonably free from slubs, snarls, and other defects.

Threads per cm : Warp not less than 16 and weft not less than 10.

Weight : 25 g has a superficial area of 1350 to 1370 sq cm.

Absorbency : A piece 10 cm square, placed lightly by means of forceps, unraised side downwards, on the surface of water at 20°, becomes saturated within 10 seconds.

Water-soluble extractive : Not more than 1.0 per cent, Appendix 3.3.22.

Fluorescence : Not more than a few points of fluorescence are visible under screened ultra-violet light.

Storage : Store in well-closed packages so as to prevent access of moisture, in a dry place, free from dust.

Labelling : The label on the container states the length and width.

Liquorice

Category : Demulcent.

Standards : Liquorice consists of the unpeeled dried root and stolons of *Glycyrrhiza glabra* Linn.

Description : Root with few branches, upto 1 m long and from 0.5 to 3 cm in diameter. The bark is brownish-grey to brown with longitudinal striations and bears traces of lateral roots. Stolons, cylindrical, upto several metres in length and 1 to 2 cm in diameter; they have the same external appearance as the roots. The fracture of the root and stolon is granular and fibrous. The cork layer is thin; secondary phloem region wide, light yellow with radial striations. Xylem cylinder compact, yellow in colour with a radiate structure. The stolon has a central pith, which is absent from the root.

Odour, characteristic and slightly aromatic; taste, very sweet and faintly astringent; the bark is not bitter.

Examined under a microscope the cork and phelloderm are narrow. Phloem consisting of bundles of thick-walled yellow fibres with narrow lumina surrounded by cells each containing a calcium oxalate prism, alternating in the external layers with areas of strongly hyaline keratenchyma; functional sieve tissue near the cambium. Medullary rays parenchymatous, widening towards the exterior, 3 to 12 cells wide. Xylem composed of radial rows of trachieds and vessels alternating with bundles of lignified fibres with crystal sheaths similar to those of the secondary phloem; vessels 30 to 150 μm in diameter, with thick walls (5 to 10 μm) having reticulate thickenings or numerous bordered pits with slit-shaped openings associated with lignified xylem parenchyma. Medullary rays 2 to 5 cells wide. Parenchymatous cells throughout containing simple, round, oval or fusiform starch granules 2 to 5 to 12 to 20 μm in diameter. Parenchymatous pith present solely in the stolon.

Identification : Mix the powdered drug with a 1 drop of *sulphuric acid*. The powder particles turn orange-yellow. Many fragments take on, more slowly, a pink-red colour.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Curcuma : When examined under a microscope, none of the fragments of the powder in *sulphuric acid* (see **Identification** test) should immediately take on a carmine-red colour.

Ash : Not more than 10.0 per cent, Appendix 3.3.22.

Acid-insoluble ash : Not more than 2.5 per cent, Appendix 3.3.22.

Water-soluble extractive : Weigh accurately about 2.5 g of the powdered drug, mix with 50 .0 ml of *water* and allow to stand for two hours, with frequent shaking. Filter and evaporate 10.0 ml of the filtrate to dryness on a water-bath and dry the residue at 105°; the residue weighs not less than 0.1 g.

Storage : Store in tightly-closed, light-resistant containers.

Lithium Carbonate

Li_2CO_3 Mol. Wt. 73.89

Category : Antidepressant.

Dose : 0.25 to 1.6 g daily in divided doses.

Description : White, crystalline powder; odourless; taste, slightly alkaline.

Solubility : Sparingly soluble in *water*; slightly soluble in boiling *water*; practically insoluble in *alcohol.*

Standards : Lithium Carbonate contains not less than 99.5 per cent of Li_2CO_3, calculated with reference to the dried substance.

Identification : (A) Dissolve 0.2 g in 5 ml of *hydrochloric acid*, boil, add 2 ml of *sodium hydroxide solution* and 5 ml of *disodium hydrogen phosphate solution* and boil; a white precipitate is produced.

(B) Moisten a small quantity with *hydrochloric acid* and introduce on a platinum wire into the flame of a Bunsen burner; a red colour is imparted to the flame.

(C) It gives the reactions of *carbonates*, Appendix 3.1.

Arsenic : Not more than 2 parts per million, Appendix 3.2.1.

Calcium and magnesium : Dissolve 1.0 g in 30 ml of *N hydrochloric acid* and neutralise with *dilute ammonia solution;* filter, if necessary, and divide into two equal portions; to one portion add 1 ml of *ammonium oxalate solution;* no turbidity or precipitate is produced on standing for five minutes; to the second portion add 1 ml of *disodium hydrogen phosphate solution*; no turbidity or precipitate is produced on standing for five minutes.

Chlorides : 1.0 g, dissolved in *water* with the addition of 5 ml of *nitric acid* complies with the *limit test for chlorides*, Appendix 3.2.2.

Heavy metals : Not more than 20 parts per million, determined by the following method: Mix 1.0 g with 5 ml of *water* and 15 ml of *dilute hydrochloric acid Sp.*, heat to boiling and maintain that temperature for one minute. Add one drop of *phenolphthalein solution*, add sufficient *ammonia solution Sp.* to give the solution a faint pink colour. Cool, and dilute to 25 ml with *water.* Proceed as described in Method A, Appendix 3.2.4.

Aluminium and iron : Dissolve 0.5 g in 10 ml of *water* by the dropwise addition, with agitation, of *hydrochloric acid.* Boil the solution, then cool it, and to 5 ml of the solution add *6N ammonia* until the reaction is alkaline; no turbidity or precipitate is observed.

Potassium : Not more than 0.1 per cent of K, determined by the following method: Dissolve 1.0 g in 10 ml of *dilute hydrochloric acid* and add sufficient *water* to produce 100.0 ml. Determine by Method A for *flame photometry*, Appendix 5.16 A, at a wavelength of 766.5 nm, using the following as the standard solution and diluting it, if necessary, with *water.*

1.1440 g of *potassium chloride*, previously dried to constant weight at 130°, dissolved in sufficient *water* to produce 1000.0 ml (This solution contains 600 µg of K in 1 ml).

Sodium : Not more than 0.2 per cent of Na, determined by the following method: Dissolve 1.0 g in 10 ml of *dilute hydrochloric acid* and add sufficient *water* to produce 100.0 ml. Determine by Method A for *flame photometry*, Appendix 5.16 A at a wavelength of 589.0 nm, using the following as the standard solution and diluting it, if necessary, with *water.*

0.5084 g of *sodium chloride*, previously dried to constant weight at 130°, dissolved in sufficient *water* to produce 1000.0 ml (This solution contains 200 µg of Na in 1 ml).

Sulphate : 1.0 g dissolved in *water* with the addition of 10 ml of *dilute hydrochloric acid* complies with the *limit test for sulphates,* Appendix 3.2.8.

Loss on drying : Not more than 0.5 per cent, determined at 105°, Appendix 5.8.

Assay : Weigh accurately about 1.0 g and suspend in 100 ml of *water.* Add 50.0 ml of *N hydrochloric acid*, boil to remove carbon dioxide, cool, and titrate the excess of acid with *N sodium hydroxide*, using *methyl orange solution* as indicator. Each ml of *N hydrochloric acid* is equivalent to 0.03695 g of Li_2CO_3.

Storage : Store in well-closed containers.

Lithium Carbonate Tablets

Category : Antidepressant.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Dose : Lithium Carbonate. Upto 1.6 g daily, in single or divided doses.

Usual strength : 300 mg.

Standards : Lithium Carbonate Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Lithium Carbonate, Li_2CO_3.

Identification : The powdered tablets comply with **Identification** test (B) described under Lithium Carbonate.

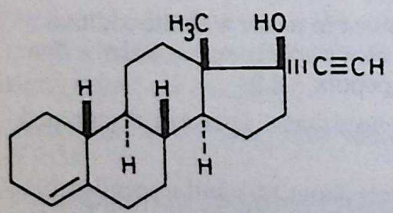
Dissolution : Carry out the *dissolution test for tablets and capsules*, Appendix 5.7, using as the medium 900 ml of *water*, and placing one tablet in the basket for each test, and rotating the basket for thirty minutes. Withdraw a sample of 90.0 ml of the medium, add a drop of *hydrochloric acid* and dilute to 100.0 ml with *water*. Determine by *flame photometry, Method A*, Appendix 5.16 A, or by *atomic absorption spectrophotometry, Method A*, Appendix 5.16 B, measuring at 671 nm, and using *lithium solution FP*, suitably diluted with *water*, for the standard solution. Not less than 60 per cent of the stated amount of Li_2CO_3 in the tablets dissolves in thirty minutes.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 1.0 g of Lithium Carbonate and carry out the **Assay** described under Lithium Carbonate.

Lynestrenol

Lynoestrenol



$C_{20}H_{28}O$ Mol. Wt. 284.42

Category : Progestin.

Dose : 2.5 to 15 mg daily.

Description : White or almost white; crystalline powder; odourless.

Solubility : Practically insoluble in *water*; soluble in *alcohol*, in *chloroform*, in *solvent ether* and in *acetone*.

Standards : Lynestrenol is 19-nor-17α-pregn-4-en-20-yn-17β-ol. It contains not less than 97.0 per cent and not more than the equivalent of 102.0 per cent of $C_{20}H_{28}O$, calculated with reference to the dried substance.

Identification : (A) The light absorption of a 1 per cent w/v solution in *methyl alcohol* exhibits no maximum in the range 230 to 350 nm, Appendix 5.15 A.

(B) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 4 volumes of *heptane* and 1 volume of *acetone* as the mobile phase but allowing the solvent front to ascend 10 cm above the line of application. Apply separately to the plate 2 µl of each of two solutions in a mixture of 9 volumes of *chloroform* and 1 volume of *methyl alcohol* containing (1) 0.25 per cent w/v of the substance being tested and (2) 0.25 per cent w/v of *lynestrenol R.S.* and at a third point apply 2 µl of a mixture of solutions (1) and (2). After removal of the plate, heat it at 105° for ten minutes, spray with a 10 per cent v/v solution of *sulphuric acid* in *alcohol*, heat at 105° for a further ten minutes, allow to cool, and examine in daylight and under an ultra-violet lamp having a maximum output at about 366 nm. The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2). The principal spot in the mixed chromatogram appears as a single, compact spot.

Melting range : Between 160° and 164°, Appendix 5.11.

Specific optical rotation : Between −8° and −13°, determined in a 5 per cent w/v solution in *dioxan*, Appendix 5.12.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 0.5 g by drying in an oven at 100° to 105°, Appendix 5.8.

Assay : Dissolve 0.2 g in 40 ml of *tetrahydrofuran*, add 10 ml of a 10 per cent w/v solution of *silver nitrate*, and titrate with *0.1 N sodium hydroxide*, determining the end-point potentiometrically. Each ml of *0.1 N sodium hydroxide* is equivalent to 0.02844 g of $C_{20}H_{28}O$.

Storage : Store in well-closed, light-resistant containers.

Milk of Magnesia

Magnesium Hydroxide Mixture

Category : Laxative; antacid.

Dose : As an antacid, 5 to 10 ml; as a laxative, 15 to 30 ml.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Description : White, uniform, suspension from which varying proportions of water may separate on standing.

Standards : Milk of Magnesia is an aqueous suspension of hydrated magnesium hydroxide. It contains not less than 7.0 per cent w/w and not more than 8.5 per cent w/w of $Mg(OH)_2$. It may contain one or more suitable preservatives.

Identification : A solution of 1 ml in 2 ml of *dilute hydrochloric acid* gives the reactions of *magnesium*, Appendix 3.1.

Alkalinity : It is alkaline to *litmus solution* and to *phenolphthalein solution*.

Microbial limits : Total microbial count does not exceed 1000 per ml and 1 ml is free from *E. coli*, Appendix 4.5.

Soluble alkalies : Filter about 25 ml and collect the middle portion of the filtrate. Dilute 5 ml of filtrate with 40 ml of *water*. Add 1 drop of *methyl red solution* and titrate with *0.1N sulphuric acid* to a persistent pink colour. Not more than 1.0 ml of *0.1N sulphuric acid* is required.

Soluble salts : To 5 ml of the clear filtrate obtained in the foregoing test add 3 drops of *sulphuric acid*. Evaporate to dryness on a water-bath and then ignite gently to constant weight; the weight of the residue does not exceed 12 mg.

Carbonates and acid-insoluble matter : To 1 ml add 2 ml of *dilute hydrochloric acid*; a slight effervescence is produced and the resulting solution is not more than slightly turbid.

Arsenic : Not more than 1 part per million, Appendix 3.2.1.

Calcium oxide : Not more than 0.1 per cent, determined by the following method: To 10.0 ml add in small portions, 25 ml of a mixture of 5 ml of *sulphuric acid* and 25 ml of *water*. Cool, add 70 ml of *alcohol* and allow the mixture to stand overnight. If crystals of magnesium sulphate separate, warm the mixture to about 50°. Filter through a Gooch crucible, prepared with asbestos, previously washed with *dilute sulphuric acid*, *water* and *alcohol*, and ignited and weighed. Wash the precipitate several times with a mixture of 2 volumes of *alcohol* and 1 volume of *2N sulphuric acid*. Dry the crucible and ignite at a dull red heat to constant weight.

Heavy metals : Not more than 5 parts per million, determined by Method A on a solution prepared in the following manner: To 5 ml add 6 ml of *dilute hydrochloric acid* and evaporate the solution to dryness on a water-bath with frequent stirring. Dissolve the residue in 20 ml of *water* and filter. Add 2 ml of *dilute acetic acid* to the filtrate and dilute to 25 ml with *water*, Appendix 3.2.4.

Assay : Weight accurately about 5 g and mix with 50 ml of *water*. Add 25.0 ml of *N sulphuric acid*, mix well and titrate the excess of acid with *N sodium hydroxide*, using *methyl red solution* as indicator. Each ml of *N sulphuric acid* is equivalent to 0.02916 g of $Mg(OH)_2$.

Storage : Store in tightly-closed containers. Do not keep in a cold place.

Labelling : The label on the containers states "Shake well before use".

Magnesium Chloride

$MgCl_2,6H_2O$ Mol. Wt. 203.30

Category : Pharmaceutical aid (for peritoneal dialysis solutions).

Description : Colourless crystals. Deliquescent.

Solubility : Freely soluble in *water* and in *alcohol*.

Standards : Magnesium Chloride contains not less than 98.0 per cent of $MgCl_2, 6H_2O$.

Identification : It gives the reactions of *magnesium* and of *chlorides*, Appendix 3.1.

Clarity and colour of solution : A 10.0 per cent w/v solution is clear and colourless.

Acidity or Alkalinity : A solution of 5.0 g in 20 ml of *water* requires for neutralisation not more than 0.1 ml of either *0.1N hydrochloric acid* or *0.1N sodium hydroxide, bromothymol blue solution* being used as indicator.

Arsenic : Not more than 2 parts per million, Appendix 3.2.1.

Barium : Dissolve 1.0 g in 10 ml of *water* and add 1 ml of *N sulphuric acid*; the solution remains clear for two hours.

Calcium : Not more than 0.01 per cent of Ca, determined by the following method: Dissolve 5.0 g in sufficient *water* to produce 100 ml and determine by Method B for *flame photometry*, Appendix 5.16 A, or by Method B for *atomic absorption spectrophotometry*, Appendix 5.16 B, measuring at 423 nm and using *calcium solution FP*, diluted if necessary, with *0.1N hydrochloric acid* for the *standard solution*.

Heavy metals : Not more than 20 parts per million, determined by Method A on a solution prepared by dissolving 1.0 g in 20 ml of *water*, adding 1 g of *ammonium chloride* and sufficient *water* to produce 25 ml, Appendix 3.2.4.

Iron : 4.0 g complies with the *limit test for iron*, Appendix 3.2.5.

Potassium : Not more than 1.0 per cent of K, determined by the following method: Dissolve 1.0 g in sufficient *water* to produce 100 ml, dilute 1 ml to 10 ml

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

with *water* and determine by Method A for *flame photometry*, Appendix 5.16 A, or by Method A for *atomic absorption spectrophotometry*, Appendix 5.16 B, measuring at 767 nm and using *potassium solution FP*, suitably diluted with *water*, for the *standard solution*.

Sodium : Not more than 0.5 per cent of Na, determined by the following method: Dissolve 1.0 g in sufficient *water* to produce 100 ml and determined by Method B for *flame photometry*, Appendix 5.16 A, or by Method B for *atomic absorption spectrophotometry*, Appendix 5.16 B, measuring at 589 nm and using *sodium solution FP*, diluted if necessary with *water* for the *standard solution*.

Phosphate : Dissolve 0.2 g in 10 ml of *water*, add 4 ml of *dilute sulphuric acid*, 1 ml of *ammonium molybdate solution*, and 2 ml of *methylaminophenol with sulphite solution*, and heat at 60° for ten minutes. Any blue colour produced is not more intense than that obtained by treating 1 ml of *potassium dihydrogen phosphate solution* in a similar manner.

Sulphate : 2.5 g complies with the *limit test for sulphates*, Appendix 3.2.8.

Assay : Weigh accurately about 0.5 g, dissolve in 50 ml of *water*, add 10 ml of *strong ammonia-ammonium chloride solution* and titrate with *0.05 M disodium ethylenediaminetetraacetate*, using 0.1 g of *mordant black 11 mixture* as indicator. Each ml of *0.05 M disodium ethylenediaminetetraacetate* is equivalent to 0.01017 g of $MgCl_2,6H_2O$.

Storage : Store in tightly-closed containers.

Heavy Magnesium Carbonate

Category : Antacid; Laxative.

Dose : As an antacid, 0.3 to 0.6 g. As a laxative, 2 to 4 g.

Description : White granular powder; odourless; tasteless. 15 g occupies a volume of about 30 ml.

Solubility : Practically insoluble in *water*, and in *alcohol*; soluble in dilute acids with effervescence.

Standards : Heavy Magnesium Carbonate is hydrated basic magnesium carbonate. It contains the equivalent of not less than 40.0 per cent and not more than 45.0 per cent of MgO.

Identification : A solution in *dilute nitric acid* gives the reactions of *magnesium*, and of *carbonates*, Appendix 3.1.

Arsenic : Not more than 2 parts per million, Appendix 3.2.1.

Calcium : Dissolve 1 g in 25 ml of a 20 per cent w/w solution of *sulphuric acid*, and add 50 ml of *alcohol*, allow to stand overnight and filter through a Gooch crucible packed with asbestos, which has been previously washed with *dilute sulphuric acid* followed by *water* until free from acid and ignited; wash the residue with 200 ml of a mixture of 2 volumes of *alcohol* and 1 volume of a 20 per cent w/v solution of *sulphuric acid*; the residue, after drying and igniting to constant weight, weighs not more than 20 mg.

Copper : Dissolve 1 g in 5 ml of *hydrochloric acid* and 25 ml of water; boil to remove carbon dioxide, make alkaline with dilute *ammonia solution*; no blue colour is produced.

Iron : Dissolve 0.1 g in 5 ml of *water* and 0.5 ml of *iron-free hydrochloric acid*; the solution complies with the *limit test for iron*, Appendix 3.2.5.

Heavy metals : Not more than 30 parts per million, determined by Method A on the following solution: Dissolve 0.67 g in 10 ml of *3 N hydrochloric acid*, and evaporate the solution on a steam-bath to dryness. Towards the end of the evaporation, stir frequently so that the residue disintegrates to a dry powder. Dissolve the residue in 20 ml of *water*, and evaporate in the same manner as before to dryness. Redissolve the residue in 20 ml of *water*, filter, if necessary, and add to the filtrate 2 ml of *N acetic acid* and *water* to make 25 ml, Appendix 3.2.4.

Chloride : Dissolve 1 g in *water* by the addition of 2 ml of *nitric acid*; the solution complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphate : Dissolve 0.2 g in *water* by the addition of 2 ml of *hydrochloric acid*; the solution complies with the *limit test for sulphates*, Appendix 3.2.8.

Soluble matter : Boil 1 g in 50 ml of *water* for five minutes, filter, evaporate the filtrate, and dry to constant weight at 105°, the residue weighs not more than 10 mg.

Residue on ignition : Not less than 42.0 per cent and not more than 45.0 per cent, determined on 0.5 g by igniting to constant weight at 900°.

Assay : Carry out the **Assay**, described under Heavy Magnesium Oxide, using 0.18 g, accurately weighed.

Storage : Store in well-closed containers.

Light Magnesium Carbonate

Category : Antacid; Laxative.

Dose : As an antacid, 0.3 to 0.6 g. As a laxative, 2 to 4 g.

Description : Very light, white powder; odourless; almost tasteless. Stable in air. Apparent volume: 15 g occupies a volume of about 125 ml.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Solubility : Practically insoluble in *water*; insoluble in *alcohol*; soluble in dilute acids with effervescence.

Standards : Light Magnesium Carbonate is a hydrated basic magnesium carbonate. It contains the equivalent of not less than 40.0 per cent and not more than 45.0 per cent of MgO.

Identification : A solution in *dilute nitric acid* gives the reactions of *magnesium*, and of *carbonates*, Appendix 3.1.

Arsenic; Calcium; Copper; Iron; Heavy metals; Soluble matter; Residue on ignition and Assay : Comply with the requirements stated under Heavy Magnesium Carbonate.

Chloride : Dissolve 0.5 g in *water* by the addition of 1.5 ml of *nitric acid*; the solution complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphate : Dissolve 0.2 g in *water* by the addition of 2 ml of *hydrochloric acid*; the solution complies with the *limit test for sulphates*, Appendix 3.2.8.

Storage : Store in well-closed containers.

Heavy Magnesium Oxide

Heavy Magnesia

MgO Mol. Wt. 40.30

Category : Antacid; Laxative.

Dose : As gastric antacid, 0.3 to 0.6 g; as a laxative, 2 to 4 g.

Description : White powder; odourless; slightly alkaline. It absorbs moisture and carbon dioxide when exposed to air. 15 g occupies a volume of about 30 ml.

Solubility : Practically insoluble in *water*; insoluble in *alcohol*; soluble in dilute acids.

Standards : Heavy Magnesium Oxide contains not less than 98.0 per cent of MgO, calculated with reference to the substance ignited at 900°.

Identification : A solution in *dilute nitric acid* gives the reaction of *magnesium*, Appendix 3.1.

Arsenic : Not more than 5 parts per million, Appendix 3.2.1.

Calcium; Copper : Comply with the tests for **Calcium** and **Copper**, described under Heavy Magnesium Carbonate, using 0.4 g.

Iron : Dissolve 40 mg in 5 ml of *water* and 0.5 ml of *iron-free hydrochloric acid*; the solution complies with the *limit test for iron*, Appendix 3.2.5.

Heavy metals : Not more than 20 parts per million, determined by Method A on the following solution: Dissolve 2 g in 20 ml of *dilute hydrochloric acid*, and evaporate the solution on a steam-bath to dryness. Towards the end of evaporation, stir frequently to disintegrate the residue so that finally a dry powder is obtained. Dissolve the residue in 20 ml of *water*, and evaporate to dryness in the same manner as before. Redissolve the residue in 20 ml of *water*, filter if necessary and dilute with *water*, to 40 ml. To 20 ml add *water* to make 25 ml, Appendix 3.2.4.

Chloride : Dissolve 0.4 g in *water* by addition of 2 ml of *nitric acid*; the solution complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphate : Dissolve 0.08 g in *water* by the addition of 2 ml of *hydrochloric acid*; the solution complies with the *limit test for sulphates*, Appendix 3.2.8.

Soluble matter : Boil 0.4 g with 50 ml of *water* for 5 minutes, filter, evaporate the filtrate, and dry to constant weight at 105°; the residue weighs not more than 10 mg.

Loss on ignition : Not more than 10.0 per cent, determined on 0.5 g by igniting to constant weight at 900°.

Assay : Weigh accurately about 0.1 g and dissolve in 2 ml of *dilute hydrochloric acid*. Add 50 ml of *water*, 10 ml of *strong ammonia-ammonium chloride solution* and titrate with *0.05M disodium ethylenediaminetetraacetate*, using 0.1 g of *mordant black II mixture* as indicator until the pink colour is discharged from the blue. Each ml of *0.05M disodium ethylenediaminetetraacetate* is equivalent to 0.002015 g of MgO.

Storage : Store in tightly-closed containers.

Light Magnesium Oxide

Light Magnesia

MgO Mol.Wt. 40.30

Category : Antacid; laxative.

Dose : As an antacid, 0.3 to 0.6 g; as a laxative, 2 to 4 g.

Description : Very light, white powder; odourless; taste, slightly alkaline. Readily absorbs moisture and carbon dioxide when exposed to air. Apparent volume, 15 g, occupies a volume of about 150 ml.

Solubility : Practically insoluble in *water*; insoluble in *alcohol*; soluble in dilute acids.

Standards : Light Magnesium Oxide contains not less than 98.0 per cent of MgO, calculated with reference to the substance ignited at 900°.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Identification : A solution in *dilute nitric acid* gives the reactions of *magnesium,* Appendix 3.1.

Arsenic; Calcium; Copper; Iron; Heavy metals; Chloride; Sulphate; Soluble matter; Loss on ignition and Assay : Comply with the tests described under Heavy Magnesium Oxide.

Storage : Store in tightly-closed containers.

Magnesium Stearate

Category : Pharmaceutical aid (lubricant).

Description : Very fine, white, light powder; odour, faint and characteristic; greasy to touch and free from grittiness.

Solubility : Insoluble in *water,* in *alcohol* and in *solvent ether.*

Standards : Magnesium Stearate is a mixture of varying proportions of magnesium stearate $[(C_{17}H_{35}COO)_2Mg]$ and magnesium palmitate $[(C_{15}H_{31}COO)_2Mg]$. It contains the equivalent of not less than 6.5 per cent and not more than 8.5 per cent of MgO.

Identification : (A) Heat 5 g with shaking, with 40 ml of *dilute sulphuric acid* and cool. Filter off the fatty acids liberated; the filtrate gives the reactions of *magnesium,* Appendix 3.1.

(B) Wash the fatty acids obtained in **Identification** test (A) with boiling *water* until the washings are free from sulphate. Collect the residue and warm on a water-bath until all the water has separated and the fatty acids are clear. Allow to cool, pour off the water layer, melt the acids and filter into a dry beaker while hot. Dry at 100° for twenty minutes; the solids so obtained melt at a temperature not below 54°, Appendix 5.11.

pH : Between 6.2 and 7.4, determined in a solution obtained by mixing 1.0 g with 20 ml of freshly boiled and cooled *water,* boiling for one minute with continuous shaking and filtering, Appendix 5.10.

Zinc stearate : Heat 5 g with shaking with a mixture of 50 ml of *water* and 50 ml of *dilute sulphuric acid* until the fatty acids separate as an oily layer. Cool, filter off the aqueous phase and wash the residue with two successive quantities, each of 5 ml, of hot *water,* combine the washings and the filtrate and dilute to 100 ml with *water.* To 5 ml of the resulting solution in a test-tube add 0.5 ml of *ammonium mercurithiocyanate solution* and one drop of a 0.1 per cent w/v solution of *copper sulphate.* Scratch the walls of the test-tube with a glass rod and allow to stand for fifteen minutes. No violet precipitate is formed.

Heavy metals : Not more than 20 parts per million, determined by the following method: Heat 5.0 g with 40 ml of *2N acetic acid* and allow to cool. Filter, wash the residue with two successive quantities, each of 5 ml, of warm *water,* and dilute the combined filtrate and washings to 100.0 ml with *water.* To 12.0 ml of the resulting solution add 1.2 ml of *thioacetamide reagent* and 2 ml of *acetate buffer, pH 3.5,* mix and allow to stand for two minutes. Any brown colour produced is not more intense than that produced by similarly treating a mixture of 1.0 ml of *standard lead solution* and 2.0 ml of the solution being examined.

Loss on drying : Not more than 6.0 per cent, determined on 0.5 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 1.0 g and boil with 50.0 ml of *0.1N sulphuric acid* for ten minutes, or until the fatty acid layer is clear, adding *water* if necessary to maintain the original volume, cool, and filter. Wash the filter and the flask with *water* until the washing is not acid to *litmus paper,* add a few drops of *methyl orange solution* and titrate the excess of acid with *0.1N sodium hydroxide.* Each ml of *0.1N sulphuric acid* is equivalent to 0.002015 g of MgO.

Storage : Store in well-closed containers.

Magnesium Sulphate

Epsom Salts

$MgSO_4, 7H_2O$ Mol.Wt. 246.47

Category : Cathartic.

Dose : 2 to 16 g.

Description : Colourless crystals, usually needle-like; odourless; taste, cool, saline and bitter. Effloresces in warm dry air.

Solubility : Freely soluble in *water*; sparingly soluble in *alcohol.* Dissolves slowly in *glycerin.*

Standards : Magnesium Sulphate contains not less than 99.0 per cent and not more than the equivalent of 100.0 per cent of $MgSO_4$, calculated with reference to the ignited substance.

Identification : A solution (1 in 20) gives the reactions of *magnesium,* and of *sulphates,* Appendix 3.1.

Clarity and colour of solution : 5 g dissolved in sufficient *water* to produce 50 ml gives a clear and colourless solution.

Acidity or Alkalinity : 1 g dissolved in 10 ml of *water* is neutral to *litmus solution.*

Arsenic : Not more than 2 parts per million, Appendix 3.2.1.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Iron : 2 g dissolved in 20 ml of *water* complies with the *limit test for iron*, Appendix 3.2.5.

Heavy metals : Not more than 10 parts per million, determined by Method A on a solution prepared by dissolving 2.0 g in 10 ml of *water*, 2.0 ml of *dilute acetic acid* and sufficient *water* to make 25 ml, Appendix 3.2.4.

Zinc : Dissolve 2 g in 20 ml of *water* and acidify with 1 ml of *acetic acid*. No turbidity is produced immediately on the addition of few drops of *potassium ferrocyanide solution*.

Chloride : 1 g complies with the *limit test for chlorides*, Appendix 3.2.2.

Loss on ignition : Between 48.0 per cent and 52.0 per cent, determined on 1.0 g by drying in an oven at 105° for two hours and igniting to constant weight at 400°.

Assay : Weigh accurately about 0.3 g and dissolve in 50 ml of *water*. Add 10 ml of *strong ammonia-ammonium chloride solution*, and titrate with *0.05M disodium ethylenediaminetetraacetate* using 0.1 g of *mordant black 11 mixture* as indicator, until the pink colour is discharged from the blue. Each ml of *0.05M disodium ethylenediaminetetraacetate* is equivalent to 0.00602 g of $MgSO_4$.

Storage : Store in well-closed containers.

Magnesium Trisilicate

Category : Antacid.

Dose : 0.5 to 2 g, repeated in accordance with the needs of the patient.

Description : Fine, white or nearly white, slightly hygroscopic powder, free from grittiness; odourless and tasteless.

Solubility : Practically insoluble in *water* and in *alcohol*.

Standards : Magnesium Trisilicate is a compound of magnesium oxide and silicon dioxide with varying proportions of water of crystallisation. It contains not less than 29.0 per cent and not more than 32.0 per cent of MgO, and not less than 65.0 per cent and not more than 68.5 per cent of SiO_2, both calculated with reference to the substance ignited at 1000°.

Identification : Boil 0.5 g with 10 ml of *sodium hydroxide solution*; filter, acidify the filtrate with *dilute hydrochloric acid* and boil; a white gelatinous precipitate is slowly produced. Wash the residue on the filter with *water*, dissolve it in *dilute hydrochloric acid* and filter; the filtrate gives the reactions of *magnesium*, Appendix 3.1.

Arsenic : Not more than 4 parts per million, Appendix 3.2.1.

Iron : Boil 50 mg with 10 ml of *water* and 1 ml of *iron-free hydrochloric acid*, filter and dilute to 40 ml with *water*; the filtrate complies with the *limit test for iron*, Appendix 3.2.5.

Heavy metals : Not more than 30 parts per million, determined by Method A on the following solution: Boil 2 g with 50 ml of *water* and 5 ml of *hydrochloric acid* for twenty minutes. Add *dilute ammonia solution* till the mixture is only slightly acid to *litmus paper*. Filter and wash with 20 ml of *water*. Combine the washings and filtrate, add two drops of *phenolphthalein solution* and then a slight excess of *dilute ammonia solution*. Discharge the pink colour with *0.1N hydrochloric acid*, then add 8 ml of *0.1N hydrochloric acid*. Dilute to 75 ml with *water* and use 25 ml of the filtrate for the test, Appendix 3.2.4.

Chloride : Boil 1 g with a mixture of 5 ml of *dilute nitric acid*, and 30 ml of *water* and filter; the filtrate complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphate : Boil 0.5 g with a mixture of 5 ml of *dilute hydrochloric acid* and 30 ml of *water* and filter; the filtrate complies with the *limit test for sulphates*, Appendix 3.2.8.

Acid-absorption : Heat 0.3 g with 100.0 ml of *0.05N hydrochloric acid* in a stoppered vessel at 37° for three hours, shaking for half a minute at fifteen minutes intervals and filter. Cool the filtrate and titrate 50.0 ml of the filtrate with *0.05N sodium hydroxide* using *methyl red solution* as indicator. Calculate the volume of *0.05N hydrochloric acid* absorbed with reference to the substance ignited at a temperature of about 1000°. 1 g of the ignited substance requires not less than 250 ml of *0.05N hydrochloric acid*.

Free alkali, soluble salts : Boil 10.0 g with 150 ml of *water* for fifteen minutes, cool and replace the water lost by evaporation. Allow to stand for fifteen minutes and filter.

Free alkali : To 15 ml of the filtrate add two drops of *phenolphthalein solution*; any pink colour is discharged on addition of 1 ml of *0.1N hydrochloric acid*.

Soluble salts : Evaporate 40 ml of the filtrate to dryness and ignite gently; the residue weighs not more than 38 mg.

Loss on ignition : Between 20 per cent and 30 per cent, determined by igniting 1.0 g at 1000° to constant weight.

Assay : *For MgO* — Weigh accurately about 1 g, add 35 ml of *hydrochloric acid* and 50 ml of *water* and allow to stand for fifteen minutes, on a water-bath. Allow to cool, filter, wash the residue with *water* and dilute the combined filtrate and washings to 250.0 ml with water. Neutralise 50.0 ml with about 8 ml of *10N sodium hydroxide*. Add 10 ml of *ammonia buffer, pH 10.0*, 50 mg of *mordant black 11 mixture*, heat to 40° and titrate with *0.05M disodium ethylenediaminetetraacetate* until the

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

colour changes from violet to full blue. Each ml of *0.05M disodium ethylenediaminetetraacetate* is equivalent to 0.002015 g of MgO.

For SiO_2 – To 0.7 g add 10 ml of *N sulphuric acid* and 10 ml of *water* and heat for one and a half hours on a water-bath with frequent shaking, replacing the evaporated *water*. Allow to cool, decant onto an ashless filter paper (diameter 7 cm), wash the precipitate by decantation with three quantities, each of 5 ml, of hot *water*, transfer it to the filter paper and wash it with hot *water* until 1 ml of the filtrate remains clear on the addition of 2 ml of *0.25M barium chloride* and 0.05 ml of *2N hydrochloric acid*. Ignite the filter paper and its contents in a tared platinum crucible at 1000° to constant weight; the residue is SiO_2.

Storage : Store in well-closed containers.

Malt Extract

Category : Nutritive.

Dose : 4 to 16 ml.

Description : Sweet, viscous, light brown liquid, having an agreeable characteristic odour.

Solubility : Almost completely soluble in cold *water*, more readily in warm *water*. An aqueous solution is not clear and deposits a voluminous flocculent precipitate on standing.

Standards : Malt Extract is a product obtained by extracting malted grains of cereals (barley, wheat or cholam) with water at a suitable temperature and evaporation of the strained liquid until a viscous product is obtained. It contains nitrogen equivalent to not less than 4.0 per cent w/w of protein. It may be mixed with 10 per cent by weight of Glycerin.

Refractive index : Between 1.489 and 1.498, determined at 20°, Appendix 5.14.

Arsenic : Not more than 1 part per million, Appendix 3.2.1.

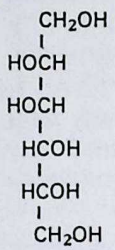
Lipase : Carry out the **Assay** *for lipase activity* described under Pancreatin, using a solution of 5 g in 10 ml of *water*. After six hours, the difference between the amount of *0.05N sodium hydroxide* added to the tubes is not more than 1.0 ml.

Assay : Weigh accurately about 5 g into a 200-ml long-necked flask and carry out the *determination of nitrogen, Method A*, Appendix 3.3.5. Each ml of *0.1N sulphuric acid* is equivalent to 0.008750 g of protein.

Storage : Store in well-closed containers, in a cool place.

Mannitol

D-Mannitol



$C_6H_{14}O_6$ Mol. Wt. 182.17

Category : Diuretic; diagnostic aid (renal function determination).

Dose : *Diuretic* – By intravenous infusion, 50 to 100 g daily in a 5 to 20 per cent solution.

Diagnostic aid – By intravenous injection, 0.2 g per kg of body weight in a 15 to 25 per cent solution.

Description : White, crystalline powder, or free-flowing granules; odourless; taste, sweet.

Solubility : Freely soluble in *water*; slightly soluble in *pyridine*; very slightly soluble in *alcohol*; insoluble in *solvent ether*.

Standards : Mannitol is a hexahydric alcohol related to mannose. It contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of $C_6H_{14}O_6$, calculated with reference to the dried substance.

Identification : (A) To 1 ml of a saturated solution, add 0.5 ml of *ferric chloride test-solution* and then 0.25 ml of *sodium hydroxide solution* and shake well. A clear solution is obtained which remains clear on the further addition of *sodium hydroxide solution*.

(B) To about 0.5 g in a test-tube add 3 ml of *acetic anhydride* and 1 ml of *pyridine*. Heat the mixture on a water-bath for fifteen minutes, with frequent shaking, or until solution is complete, and continue heating for five minutes. Cool the mixture, add 20 ml of *water*, mix, allow to stand for five minutes and collect the precipitate on a sintered glass, filter; the precipitate so obtained, after being dried "in vacuo at 60°" for 1 hour or after recrystallisation from *solvent ether*, melts between 119° and 120°, Appendix 5.11.

Melting range : Between 165° and 169°, Appendix 5.11.

Specific optical rotation : Between +23° and +24°, determined in a solution prepared by adding to 5.0 g, 6.4 g of *borax* and sufficient *water* to produce about 45 ml, allowing to stand for one hour with occasional shaking, and dilute to 50.0 ml with *water*, Appendix 5.12.

Acidity : 5.0 g dissolved in 50 ml of *carbon dioxide-free water*, requires for neutralization not more than 0.3 ml of

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

0.02N sodium hydroxide, phenolphthalein solution being used as indicator.

Chloride : 5.0 g complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphate : 5.0 g complies with the *limit test for sulphates*, Appendix 3.2.8.

Arsenic : Not more than 2 parts per million, Appendix 3.2.1.

Absence of reducing sugars : To 5 ml of *alkaline cupric citrate solution* add 1 ml of a saturated solution of Mannitol. Heat for 5 minutes in a boiling water-bath; not more than a very slight precipitate is formed.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined by drying 1.0 g in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.4 g and dissolve in sufficient *water* to produce 100.0 ml. Transfer 10.0 ml to a stoppered flask, add 20.0 ml of a 2.14 per cent w/v solution of *sodium periodate* and 2 ml of *dilute sulphuric acid*, and heat on a water-bath for fifteen minutes. Cool, add 3 g of *sodium bicarbonate* and 25 ml of *0.2N sodium arsenite*, mix, add 5 ml of a 20 per cent w/v solution of *potassium iodide*, allow to stand for fifteen minutes, and titrate with *0.1N iodine* until the first trace of yellow colour appears. Repeat the operation without the mannitol; the difference between the titrations represents the amount of *0.1N iodine* required. Each ml of *0.1N iodine* is equivalent to 0.001822 g of $C_6H_{14}O_6$.

Storage : Store in well-closed containers.

Measles Vaccine Live

Measles Vaccine (live attenuated)

Category : Active immunising agent.

Dose : Pediatric, by subcutaneous injection, 0.5 ml of reconstituted vaccine.

Standards : Measles Vaccine Live is a bacterially sterile aqueous suspension of a suitable live, attenuated strain of measles virus grown on cultures of chick embryo cells. It is reconstituted from a freeze-dried product immediately before use by adding to it the appropriate quantity of Water for Injection. It does not contain any added bactericide.

The strain of attenuated measles virus used in the manufacture of live vaccine is tested on monkeys for freedom from neurovirulence, for safety and for immunogenicity, and found suitable for human immunisation in adequate clinical trials. The final vaccine represents not more than ten sub-cultures from the vaccine on which tests for suitability were made.

The strain is grown with aseptic precautions in cultures of chick embryo cells that have not been propagated in series. The chick embryos are derived from healthy, pathogen-free flocks and the cell cultures are shown not to contain extraneous micro-organisms. Only primary cell tissue cultures are used in the manufacture of the vaccine. The medium for maintaining cell growth, as distinct from that for initiating it, contains no serum but may contain a suitable pH indicator.

The harvesting of the virus is done within fourteen days of inoculation and the virus suspension is tested for identity, sterility and freedom from adventitious viral agents. Harvests which pass these tests are pooled and clarified to remove intact tissue cells. A suitable stabiliser is added to the clarified vaccine and it is then distributed into sterile containers and freeze-dried before the containers are sealed.

NOTE – The manufacturing method or process or the conditions under which it is conducted as given in the above Standards may be modified provided the manufacturer presents to the Licensing Authority under the Drug & Cosmetic Rules, 1945, evidence to show that the modification will provide assurance of the Safety, Purity and Potency of the vaccine that are equal to or greater than the assurance provided by these Standards.

Description : White or nearly white, friable mass.

Identification : When neutralised with measles virus antiserum the reconstituted vaccine is unable to infect susceptible tissue cultures.

The reconstituted vaccine complies with the following requirements:

Freedom from adventitious viral agents – When neutralised with type-specific measles antiserum, the neutralised mixture, when inoculated into human and simian cell tissue culture systems does not produce changes in the cultures attributable to growth of adventitious viral agents.

Sterility : Complies with the *tests for sterility*, Appendix 4.6.

Undue toxicity : Complies with the *test for undue toxicity for vaccines and sera*, Appendix 2.37.

Potency : Titrate for live measles virus in a suitable cell culture system, free of wild viruses, using, *standard measles vaccine live* as a titration control. The concentration of live measles vaccine shall be not less than the equivalent of 1000 $TCID_{50}$ (quantity of virus, estimated to

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

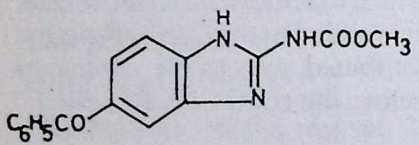
Digitized by Arya Samaj Foundation Chennai and eGangotri

inject 50 per cent of inoculated cultures × 1000) of the *standard measles vaccine live* per immunizing dose.

Storage : Store in single-dose, light-resistant containers at a temperature between 2° and 8°. The reconstituted vaccine should be used, immediately after preparation.

Labelling : The label on the container states (1) that the vaccine is freeze-dried; (2) the storage conditions; (3) the date after which it is not intended to be used; (4) "Chick embryo culture"; (5) the volume of Water for Injection to be used for reconstitution; (6) "To be used immediately after reconstitution"; (7) the strain of the virus used; (8) the virus titre.

Mebendazole



$C_{16}H_{13}N_3O_3$ Mol.Wt. 295.30

Category : Anthelmintic.

Dose : For threadworm infestation, 100 mg as a single dose; for other infestations, 100 mg twice daily for two days.

Description : White to slightly yellow amorphous powder; almost odourless.

Solubility : Practically insoluble in *water* and in most organic solvents; freely soluble in *formic acid.*

Standards : Mebendazole is Methyl 5-benzoylbenzimidazol-2-yl-carbamate. It contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of $C_{16}H_{13}N_3O_3$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *mebendazole R.S.*, Appendix 5.15 B.

(B) It melts at about 290°, Appendix 5.11.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel GF 254* as the coating substance and a mixture of 90 volumes of *chloroform*, 5 volumes of *methyl alcohol* and 5 volumes of *anhydrous formic acid* as the mobile phase. Apply separately to the plate 10 µl of each of the following solutions: (1) dissolve 50 mg of the substance being examined in 1 ml of *anhydrous formic acid* and sufficient *chloroform* to produce 10 ml; (2) a 0.5 per cent w/v solution of *mebendazole R.S.* in a mixture of 9 volumes of *chloroform* and 1 volume of *anhydrous formic acid*; (3) a 0.0025 per cent w/v solution of *mebendazole R.S.* in the same solvent mixture. After removal of the plate, allow it to dry in air and examine it under an ultra-violet lamp having a maximum output at about 365 nm. The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2). No spot other than the principal spot in the chromatogram obtained with solution (1) is larger or more intensely coloured than the main spot in the chromatogram obtained with solution (3).

Heavy metals : Not more than 20 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105° for four hours, Appendix 5.8.

Assay : Weigh accurately about 0.25 g and dissolve in 30 ml of *glacial acetic acid.* Titrate with *0.1N perchloric acid*, determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02953 g of $C_{16}H_{13}N_3O_3$.

Storage : Store in well-closed containers.

Mebendazole Tablets

Category : Anthelmintic.

Dose : Mebendazole. For threadworm infestation, 100 mg as a single dose; for other infestations, 100 mg twice daily for two or three days.

Usual strength : 100 mg.

Standards : Mebendazole Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Mebendazole, $C_{16}H_{13}N_3O_3$.

Identification : Shake a quantity of the powdered tablets equivalent to 50 mg of Mebendazole with a mixture of 1 ml of *anhydrous formic acid* and 9 ml of *chloroform* for thirty minutes, filter and evaporate the filtrate to dryness. The *infra-red absorption spectrum* of the residue exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to those in the spectrum of *mebendazole R.S.*, Appendix 5.15 B.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel GF 254* as the coating substance and a mixture of 90 volumes of *chloroform*, 5 volumes of *methyl alcohol* and

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

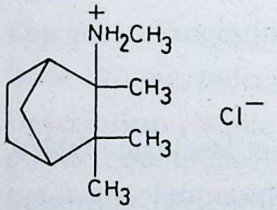
5 volumes of *anhydrous formic acid* as the mobile phase. Apply separately to the plate 10 µl of each of the following solutions: (1) Shake a quantity of the powdered tablets equivalent to 50 mg of Mebendazole with a mixture of 1 ml of *anhydrous formic acid* and 9 ml of *chloroform* and filter; (2) A 0.0025 per cent w/v solution of *mebendazole R.S.* in the same solvent mixture. After removal of the plate, allow it to dry in air and examine it under an ultraviolet lamp having a maximum output at about 254 nm. Any spot in the chromatogram obtained with solution (1), other than the principal sopt is not more intense than the spot in the chromatogram obtained with solution (2).

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powdered tablets equivalent to 0.25 g of Mebendazole and dissolve in 30 ml of *glacial acetic acid.* Titrate with *0.1N perchloric acid*, determining the endpoint potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02953 g of $C_{16}H_{13}N_3O_3$.

Storage : Store in a well-closed container.

Mecamylamine Hydrochloride



$C_{11}H_{21}N, HCl$ Mol. Wt. 203.75

Category : Antihypertensive.

Dose : Initial dose, 5 mg daily, in divided doses; subsequent doses, in accordance with the needs of the patient.

Description : White crystalline powder; odourless or almost odourless; tasteless.

Solubility : Soluble in *water* and in *chloroform;* practically insoluble in *solvent ether.*

Standards : Mecamylamine Hydrochloride is methyl-2,3,3′-trimethylbicyclo [2.2.1] hept-2-ylamine hydrochloride. It contains not less than 95.0 per cent and not more than the equivalent of 100.5 per cent of $C_{11}H_{21}N, HCl$, calculated with reference to the dried substance.

Identification : (A) To 10 ml of a 1 per cent w/v solution, add 10 ml of *alkaline picric acid solution;* a precipitate is formed which, after washing with *water* and drying has a melting range between 189° and 191°, with decomposition, Appendix 5.11.

(B) It melts at about 245° with decomposition, Appendix 5.11.

(C) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

Acidity : 2 g dissolved in 20 ml of *carbon dioxide-free water* requires for neutralisation not more than 0.2 ml of *0.1N sodium hydroxide*, using, *methyl red solution* as indicator.

Heavy metals : Not more than 50 parts per million, determined by Method A in a solution prepared by dissolving 0.4 g in 20 ml of *water*, and 2 ml of *dilute acetic acid* and sufficient *water* to produce 25 ml, Appendix 3.2.4.

Chloride : Not less than 17.0 per cent and not more than 17.8 per cent, determined by the following method: Weigh accurately about 0.5 g and dissolve in 5 ml of *water.* Add 5 ml of *glacial acetic acid,* 50 ml of *methyl alcohol* and one drop of *eosin solution* and titrate with *0.1N silver nitrate.* Each ml of *0.1N silver nitrate* is equivalent to 0.003546 g of Cl.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying "in vacuo" for one hour at 100°, Appendix 5.8.

Assay : Weigh accurately about 0.5 g and dissolve in 25 ml of *water,* add 1 ml of *sodium hydroxide solution* and extract with five successive quantities, each of 25 ml, of *chloroform.* Combine the extracts and wash with 15 ml of *water*, and extract the washings with two successive quantities, each of 10 ml, of *chloroform.* To the combined extracts and washings, add 50.0 ml of *0.1N sulphuric acid,* evaporate off the *chloroform* and titrate the excess acid with *0.1N sodium hydroxide*, using *methyl red solution* as indicator. Each ml of *0.1N sulphuric acid* is equivalent to 0.02038 g of $C_{11}H_{21}N, HCl$.

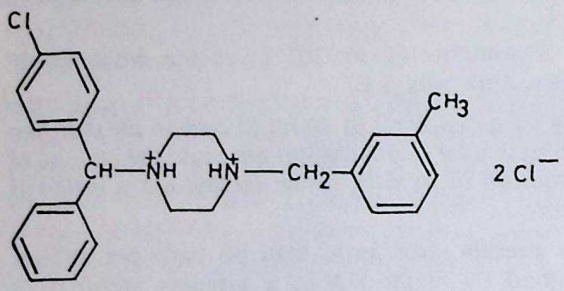
Storage : Store in well-closed containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Meclizine Hydrochloride

Meclozine Hydrochloride



$C_{25}H_{27}ClN_2$, 2HCl Mol. Wt. 463.88

Category : Antihistaminic; anti-emetic.

Dose : 25 to 50 mg daily.

Description : White or slightly yellowish, crystalline powder; odour, slight; tasteless.

Solubility : Practically insoluble in *water* and in *solvent ether*; slightly soluble in *alcohol*; very soluble in *chloroform* and in acid-alcohol-water mixtures.

Standards : Meclizine Hydrochloride is the dihydrochloride of 1-(4-chlorobenzhydryl)-4-(3-methylbenzyl) piperazine. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_{25}H_{27}ClN_2$, 2HCl, calculated with reference to the anhydrous substance.

Identification : (A) Dissolve 0.2 g in 25 ml of *alcohol* and add 25 ml of a saturated solution of *picric acid* in *alcohol* and filter; the precipitate, after washing with *water* and drying at 105° melts at about 218° with decomposition, Appendix 5.11.

CAUTION – Picrates may explode if heated too rapidly.

(B) The light absorption, in the range 220 to 350 nm, of a 1-cm layer of a 0.0015 per cent w/v solution in *alcohol* exhibits a maximum only at 230 nm; *extinction* at 230 nm, about 0.495, Appendix 5.15 A.

(C) Dissolve 25 mg in a mixture of 3 ml of *dilute nitric acid* and 5 ml of *alcohol*; the solution gives the reactions of *chlorides*, Appendix 3.1.

Melting range : Between 217° and 224°, with decomposition, Appendix 5.11.

N-(3-methylbenzyl) piperazine : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 75 volumes of *cyclohexane*, 15 volumes of *toluene* and 10 volumes of *diethylamine* as the mobile phase. Apply separately to the plate 10 µl of each of the following two solutions: (1) a 10 per cent w/v solution of the substance being examined in a mixture of equal volumes of *chloroform* and *methyl alcohol*; (2) a 0.05 per cent w/v solution of *N-(3-methylbenzyl) piperazine R.S.* in *methyl alcohol*. After removal of the plate, dry it at 100° for thirty minutes and spray consecutively with equal volumes of the following solutions: (1) A mixture of 1 volume of a 10 per cent w/v solution of *sodium hydroxide*, 1 volume of a 10 per cent solution of *sodium nitroprusside*, 1 volume of a 10 per cent w/v solution of *potassium ferricyanide* and three volumes of *water*; (2) *acetone*. The spot in the chromatogram obtained with solution (2) is more intense than the corresponding spot in the chromatogram obtained with solution (1).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Water : Not more than 5.0 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately about 0.35 g, dissolve in 50 ml of *chloroform*, add 50 ml of *glacial acetic acid*, 5 ml of *acetic anhydride* and 12 ml of *mercuric acetate solution* and titrate with *0.1N perchloric acid* using a 0.1 per cent w/v solution of *quinaldine red* in *glacial acetic acid* as indicator. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02319 g of $C_{25}H_{27}ClN_2$, 2HCl.

Storage : Store in well-closed containers.

Meclizine Tablets

Meclizine Hydrochloride Tablets; Meclozine Tablets

Category : Antinauseant; antihistaminic.

Dose : Meclizine Hydrochloride 25 to 50 mg once a day.

Usual strength : 25 mg.

Standards : Meclizine Tablets contain not less than 95.0 per cent and not more than 110.0 per cent of the stated amount of Meclizine Hydrochloride, $C_{25}H_{27}ClN_2$, 2HCl.

Identification : Triturate a quantity of the powdered tablets equivalent to about 0.35 g of Meclizine Hydrochloride with three quantities, each of 10 ml, of *chloroform*. Filter the extracts and evaporate the clear filtrate on a water-bath to dryness; the residue so obtained complies with **Identification** tests (A) and (B) described under Meclizine Hydrochloride.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and reduce to fine powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.35 g of Meclizine Hydrochloride and extract with

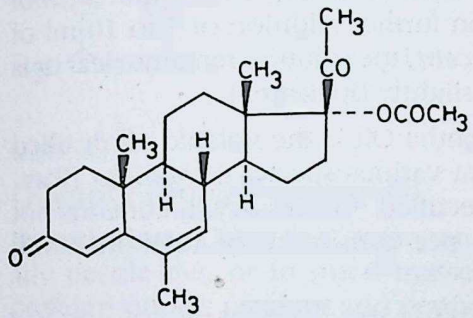
CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

three quantities, each of 50 ml, of *chloroform*, stirring the mixture each time for thirty minutes, then allowing the undissolved matter to settle and decanting the supernatant liquid on to a fine, sintered-glass filter. Transfer the residue to the filter with the aid of *chloroform* and wash the vessel and filter with 20 ml of *chloroform*. Combine the extracts and washing and evaporate on a water-bath to 10 ml. Cool, and carry out the **Assay**, described under Meclizine Hydrochloride, beginning at the words "add 50 ml of *glacial acetic acid*....."

Storage : Store in well-closed containers.

Megestrol Acetate



$C_{24}H_{32}O_4$ Mol. Wt. 384.52

Category : Progestin.

Dose : 20 mg, twice daily.

Description : White to creamy-white, crystalline powder; odourless.

Solubility : Practically insoluble in *water*; sparingly soluble in *alcohol*; slightly soluble in *solvent ether* and in fixed oils; very soluble in *chloroform*.

Standards : Megestrol Acetate is 6-methyl-17α- hydroxy-4, 6-pregnadien-3,20-dione 17-acetate. It contains not less than 97.0 per cent and not more than the equivalent of 103.0 per cent of $C_{24}H_{32}O_4$, calculated with reference to the dried substance.

Identification : (A) Complies with the test for *identification of steroids*, Appendix 3.3.11, using *solvent II* and *mobile phase D* and applying to the chromatoplate 1 µl of each of the solutions.

(B) To about 15 mg in a test-tube add three drops of *phosphoric acid*, close the tube with a stopper through which passes a smaller test-tube filled with water and on the outside of which hangs a drop of *lanthanum nitrate solution*. Heat in a water-bath for five minutes, mix the drop of *lanthanum nitrate solution* with a drop of *0.02 N iodine* on a white tile, and place at the edge of the mixture a drop of *dilute ammonia solution*. A blue colour slowly appears at the junction of the two liquids.

(C) It melts at about 217°, Appendix 5.11.

Specific optical rotation : Between +9° and +12°, determined at 20° in a 5 per cent w/v solution in *chloroform*, Appendix 5.12.

Light absorption : The light absorption, in the range 230 to 350 nm of 1-cm layer of the solution obtained in the **Assay** exhibits a maximum only at about 287 nm; ratio of the *extinction* at 240 nm to that at the maximum at about 287 nm, not more than 0.15, Appendix 5.15 A.

Related foreign steroids : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 92 volumes of *ethylene chloride*, 8 volumes of *methyl alcohol* and 0.5 volume of *water* as the mobile phase. Apply separately to the plate 1 µl of each of two solutions in a mixture of 9 volumes of *chloroform* and 1 volume of *methyl alcohol*, containing (1) 5 per cent w/v of the substance being tested and (2) 0.025 per cent w/v of *megestrol R.S.* After removal of the plate, allow the solvent to evaporate at room temperature, spray with a 10 per cent v/v solution of *sulphuric acid* in *alcohol*, heat at 110° for ten minutes, and examine under an ultra-violet lamp having a maximum output at about 366 nm. Any spot in the chromatogram obtained with solution (1), other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (2).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

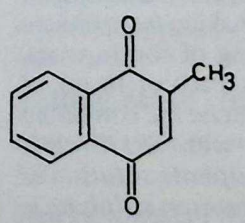
Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 10 mg and dissolve in sufficient *ethyl alcohol* to produce 100.0 ml. Dilute 5.0 ml to 50.0 ml with *ethyl alcohol* and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 287 nm, Appendix 5.15 A. Calculate the content of $C_{24}H_{32}O_4$, from the *extinction* obtained by repeating the operation on 10 mg, accurately weighed, of *megestrol acetate R.S.*

Storage : Store in well-closed, light-resistant containers.

Menadione

Menaphthone



$C_{11}H_8O_2$ Mol. Wt. 172.18

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Category : Prothrombogenic vitamin (source of Vitamin K).

Description : Bright yellow, crystalline powder; odour, faint and characteristic. It is irritating to mucous membrane and skin. It decomposes on exposure to light, darkening in colour to light brown.

Solubility : Practically insoluble in *water*; sparingly soluble in *alcohol* and in *chloroform.*

Standards : Menadione is 2-methyl-1, 4-naphtha lenedione. It contains not less than 98.5 per cent of $C_{11}H_8O_2$, calculated with reference to the dried substance.

Identification : (A) To 0.5 mg dissolved in 5 ml of *alcohol*, add 2 ml of *dilute ammonia solution* and a few drops of *ethyl cyanoacetate*; a violet colour is produced. Divide the solution in two parts. To one part add 5 ml of *sodium hydroxide solution*; a brownish-yellow colour is produced. To the other part add acid or expose to sunlight; the violet colour is destroyed.

(B) The light absorption, in the range 220 to 350 nm of a 1-cm layer of a 0.0005 per cent w/v solution in *alcohol* exhibits a maximum only at 250 nm, Appendix 5.15 A.

Melting range : Between 105° and 107°, Appendix 5.11.

Chromium : Incinerate 0.5 g in a platinum crucible and fuse the residue with about 10 mg of a mixture of 1.75 parts of *potassium carbonate*, 1.35 parts of *anhydrous sodium carbonate*, and 1 part of *sodium peroxide;* cool, dissolve the residue in 10 ml of *water*, acidify the solution with *dilute sulphuric acid*, and add sufficient *water* to produce 25 ml. To 5 ml of this solution add 4 drops of *diphenylcarbazide solution* and sufficient *water* to produce 10 ml; the violet colour produced is not deeper than that produced by acidifying 1 ml of 0.00283 per cent w/v solution of *potassium dichromate* with *dilute sulphuric acid*, adding 4 drops of *diphenylcarbazide solution* and sufficient *water* to produce 10 ml.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7

Loss on drying : Not more than 0.5 per cent, determined on 1 g by drying "in vacuo" for four hours, Appendix 5.8.

Assay : Weigh accurately about 0.15 g in a flask, dissolve in 15 ml of *glacial acetic acid*, add 15 ml of *dilute hydrochloric acid*, 1 g of *zinc powder*, close the flask with a stopper fitted with a Bunsen valve, and allow the mixture to react for sixty minutes in the dark, shaking from time to time Filter the solution through a plug of cotton wool, wash with three successive quantities, each of 10 ml, of freshly boiled and cooled *water*, and titrate the combined filtrate and washings immediately with *0.1N ceric ammonium sulphate* using *ferrous sulphate solution* as indicator. Each ml of *0.1N ceric ammonium sulphate* is equivalent to 0.00861 g of $C_{11}H_8O_2$.

Storage : Store in well-closed, light-resistant containers.

Mentha Oil

Mentha

Category : Carminative.

Dose : 0.06 to 0.2 ml.

Description : Colourless or yellowish, clear liquid; odour characteristic, pleasant; taste, pungent, followed by a cooling sensation.

Solubility : 1 ml dissolves in 3.5 to 4 ml of *alcohol (70 per cent)*, on further addition of 5 to 10 ml of *alcohol (70 per cent)* the solution remains clear or is not more than slightly opalescent.

Standards : Mentha Oil is the volatile oil distilled with steam from various species of *Mentha* (Fam. Labiatae) and rectified if necessary. It contains not less than 50.0 per cent w/w of total menthol, $C_{10}H_{20}O$.

Acidity or Alkalinity : The solution of 1 ml in 3.5 ml of *alcohol (70 per cent)* is neutral to *litmus.*

Wt. per ml : Between 0.892 and 0.910 g, Appendix 5.19.

Optical rotation : Between −18° and −33°, Appendix 5.12.

Assay : Place 10 g in an acetylation flask, add 10 ml of *acetic anhydride* and 1 g of *anhydrous sodium acetate*, attach a reflux condenser, and boil for two hours. Cool, add 30 ml of *water*, and warm on a water-bath for fifteen minutes with occasional shaking. Transfer the contents of the flask to a separator, reject the water layer and wash the remaining oil with *water* until the last washing no longer shows acid reaction. Dry the resulting oil by shaking with 2 g of *anhydrous sodium sulphate*, allow it to stand for thirty minutes and filter through a dry filter paper Weigh accurately 1 to 2g of this dry acetylated oil, add 3 ml of *alcohol* and two drops of *phenolphthalein solution* and drop by drop *0.5N alcoholic potassium hydroxide* until the solution acquires a faint pink colour. Add a further 20.0 ml of the alkali, attach a reflux condenser, and boil for one hour on a water-bath. Cool, add 1 ml of *phenolphthalein solution* and titrate the excess alkali with *0.5N hydrochloric acid.* Repeat the experiment with the same quantities of the same reagents in the same manner omitting the oil and calculate the amount of total menthol from the following formula:

$$\text{Total menthol (in per cent)} = \frac{(a-b) \times 7.813}{S-(a-b) \times 0.021}$$

where S is the amount in grams of the acetylated sample

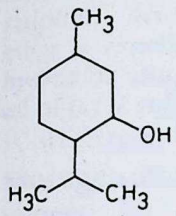
CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

taken, a the amount in ml of *0.5N hydrochloric acid* consumed in blank test, and b the amount in ml of *0.5N hydrochloric acid* consumed in saponification of the acetylated oil tasted.

Storage : Store in well-closed, light-resistant containers.

Menthol



$C_{10}H_{20}O$ Mol. Wt. 156.27

Category : Topical antipruritic.

Description : Colourless, hexagonal crystals, usually needle-like, or in fused masses or crystalline powder; odour, pleasant and peppermint-like.

Solubility : Slightly soluble in *water*; very soluble in *alcohol*, in *chloroform* and in *solvent ether*; freely soluble in *light liquid paraffin* and in *glacial acetic acid*, and in essential oils.

Standards : Menthol is 2-isopropyl-5-methylcyclohexanol. It is natural laevo-menthol obtained from various species of *Mentha*, or synthetic laevo-menthol or racemic menthol.

Identification : (A) Dissolve 10 mg in 1 ml of *sulphuric acid* and add 1 ml of a 1 per cent w/v solution of *vanillin* in *sulphuric acid*; an orange-yellow colour is produced; on adding 1 ml of *water* the colour changes to violet (distinction from thymol).

(B) Dissolve a few crystals in 1 ml of *glacial acetic acid*, add three drops of *sulphuric acid* and one drop of *nitric acid*; no green colour is developed (distinction from thymol).

(C) When triturated with about an equal weight of *camphor*, or of *chloral hydrate* or of *phenol*, the mixture liquefies.

Acidity or Alkalinity : A solution in *alcohol* is neutral to *litmus solution*.

Non-volatile matter : Not more than 0.05 per cent, when heated on a water-bath in an open dish and dried to constant weight at 105°.

Melting range of natural or synthetic laevo-menthol : Between 42° and 44°, Appendix 5.11.

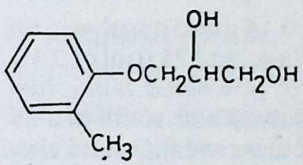
Specific optical rotation of natural or synthetic laevo-menthol : Between −49° and −50°, determined in a 10 per cent w/v solution in *alcohol*, Appendix 5.12.

Congealing range of racemic menthol : Between 27° and 28°; on prolonged stirring the temperature rises between 30° and 32°, Appendix 5.5.

Storage : Store in well-closed containers at a temperature not above 30°.

Labelling : The label on the container states whether it is laevo-menthol or racemic menthol.

Mephenesin



$C_{10}H_{14}O_3$ Mol. Wt. 182.22

Category : Skeletal muscle relaxant.

Dose : By intravenous infusion, 0.1 to 1 g.

Description : White, crystalline powder; almost odourless; taste, bitter and followed by local numbness.

Solubility : Slightly soluble in *water*; freely soluble in *alcohol*, in *chloroform* and in *solvent ether*.

Standards : Mephenesin is 3-(2-methylphenoxy)-1, 2-propanediol. It contains not less than 99.0 per cent of $C_{10}H_{14}O_3$, calculated with reference to the dried substance.

Identification : (A) Dissolve 10 mg in about 0.5 ml of *sulphuric acid*; a pink colour develops which turns intense red on the addition of one drop of 3 per cent solution of *formaldehyde*.

(B) Suspend about 100 mg in 2 ml of a 5 per cent w/v solution of *sodium hydroxide*, add 2 ml of *0.1N potassium permanganate*, and warm the mixture until the green colour changes to brown. Add 5 ml of *water*; mix and filter. To the filtrate add a few drops of *diazotised p-nitroaniline solution*; a deep red colour is produced which disappears on acidification with *dilute hydrochloric acid*.

Melting range : Between 70° and 73°, Appendix 5.11.

Arsenic : Not more than 10 parts per million, Appendix 3.2.1.

Heavy metals : Not more than 20 parts per million, determined by Method A on a solution prepared by

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

dissolving 1 g in 5 ml of *glacial acetic acid* and 15 ml of *water* and adding *dilute ammonia solution* to pH 4, and diluting with *water* to 25 ml, Appendix 3.2.4.

Chloride : Shake 2.5 g with 50 ml of *water* and filter, 40 ml of filtrate complies with the *limit test for chlorides*, Appendix 3.2.2.

***o*-Cresol :** To 10 ml of a 1 per cent w/v solution add three drops of *diazotised p-nitroaniline solution* and 2 ml of *sodium hydroxide solution*. The colour produced is less intense than that produced by a solution of 1 mg of *o-Cresol* in 10 ml of *water*, treated in the same manner.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying "in vacuo" for twenty-four hours, Appendix 5.8.

Assay : Weigh accurately about 0.15 g and dissolve in 50 ml of *water* in a glass-stoppered flask. Add 25.0 ml of *0.1N potassium bromate* and 10 g of powdered *potassium bromide*. When the latter is dissolved add 10 ml of a 25 per cent w/v *hydrochloric acid*, close the flask, and after 10 seconds add 10 ml of *potassium iodide solution*. Titrate with *0.1N sodium thiosulphate*, using *starch solution* as indicator. Each ml of *0.1N potassium bromate* is equivalent to 0.009111 g of $C_{10}H_{14}O_3$.

Storage : Store in well-closed containers and avoid exposure to excessive heat.

Mephenesin Injection

Category : Skeletal muscle relaxant.

Dose : By intravenous infusion, 1 to 10 ml.

Standards : Mephenesin Injection is a solution of Mephenesin in a mixture of Alcohol, Propylene Glycol and Water for Injection. It contains not less than 9.5 per cent and not more than 10.5 per cent w/v of Mephenesin, $C_{10}H_{14}O_3$.

Identification : (A) Dilute 1 ml with *water* to 100 ml, and dilute 5 ml of the solution to 100 ml with *water*; *extinction* of a 1-cm layer of the resulting solution at 270 nm, about 0.4, Appendix 5.15 A.

(B) Melting range of the residue from the **Assay**, between 68° and 72°, Appendix 5.11.

Alcohol content : 22 to 25 per cent v/v, Appendix 5.2 A.

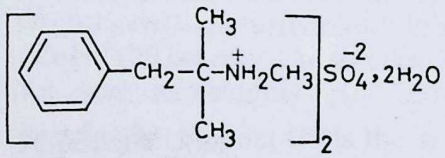
Other requirements : Complies with the requirements described under Injections.

Assay : Measure accurately 5 ml and dilute with *water* to 25 ml and extract with 20 ml of *chloroform*. Continue the extraction with further six quantities, each of 20 ml, of *chloroform* and continue the extraction till mephenesin is completely extracted, washing each *chloroform* extract with the same 5 ml of *water*. Combine the extracts, evaporate the *chloroform*, and dry the residue of $C_{10}H_{14}O_3$ to constant weight in vacuum over *phosphorus pentoxide* at 60°.

Storage : Store in single-dose containers in a cool place.

Labelling : The label on the container states that any solid matter that has separated on standing should be redissolved by warming before use.

Mephentermine Sulphate



$(C_{11}H_{17}N)_2, H_2SO_4, 2H_2O$ Mol. Wt. 460.63

Category : Adrenergic (used in the treatment of hypotension).

Dose : By intravenous or intramuscular injection, 20 to 80 mg.

Description : White crystals or crystalline powder; odourless.

Solubility : Soluble in *water*; slightly soluble in *alcohol*.

Standards : Mephentermine Sulphate is the dihydrate of *N*-methyl-*N*-(2-methyl-3-phenyl-2-propyl) ammonium sulphate. It contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of $(C_{11}H_{17}N)_2, H_2SO_4$, calculated with reference to the dried substance.

Identification : (A) A 0.2 per cent w/v solution yields precipitate with *iodide solution* and with *potassium mercuri-iodide solution*.

(B) Dissolve 0.1 g in 5 ml of *water*, add with stirring 10 ml of *picric acid solution*. Set aside for thirty minutes, filter and wash the precipitate with small portions of cold *water* until the last washing is colourless; the precipitate so obtained, after drying at 105°, melts between 154° and 158°, Appendix 5.11.

(C) A solution (1 in 20) gives the reaction of *sulphates*, Appendix 3.1.

pH : Between 4.0 and 6.5, determined in a 2.0 per cent w/v solution, Appendix 5.10.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Loss on drying : Between 5.0 per cent and 8.0 per cent, determined on 1.0 g by drying in an oven at 105° for three hours, Appendix 5.8.

Assay : Weigh accurately about 0.4 g and dissolve in 280 ml of *water*. Add 5 g of *sodium chloride*, shake well and add 5 ml of *sodium hydroxide solution*. Extract with 30 ml and then with further quantities, each of 20 ml, of *solvent ether* until the base is completely extracted. Combine the ether extracts, wash with two quantities, each of 10 ml, of *water* and extract the aqueous washings with 10 ml of *solvent ether*, adding this ether to the main ether layer. Add to the ether solution 30.0 ml of *0.1N sulphuric acid*, stir thoroughly and warm gently until ether is expelled. Cool and titrate with *0.1N sodium hydroxide* using *methyl red solution* as indicator. Each ml of *0.1N sulphuric acid* is equivalent to 0.02123 g of $(C_{11}H_{17}N)_2, H_2SO_4$.

Storage : Store in well-closed, light-resistant containers.

Mephentermine Injection

Category : Adrenergic (used in the treatment of hypotension).

Dose : By intramuscular or slow intravenous injection, the equivalent of 20 to 80 mg of mephentermine base.

Usual strength : The equivalent of 15 mg of mephentermine base per ml.

Standards : Mephentermine Injection is a sterile solution of Mephentermine Sulphate in Water for Injection. It contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Mephentermine, $C_{11}H_{17}N$.

Identification : Complies with **Identification** tests (A) and (B) described under Mephentermine Sulphate.

pH : Between 4.0 and 6.5, Appendix 5.10.

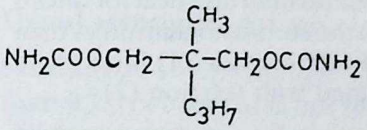
Other requirements : Complies with the requirements stated under Injection.

Assay : Measure accurately a volume equivalent to about 0.2 g of Mephentermine Sulphate, add *water* if necessary to produce 20 ml and carry out the **Assay** described under Mephentermine Sulphate, beginning at the words "add 5 g of *sodium chloride*" but using 15.0 ml of *0.1N sulphuric acid*. Each ml of *0.1N sulphuric acid* is equivalent to 0.008163 g of $C_{11}H_{17}N$.

Storage : Store in single-dose or multiple-dose, light-resistant containers.

Labelling : The label on the container states the strength in terms of the equivalent amount of mephentermine base.

Meprobamate



$C_9H_{18}N_2O_4$ Mol. Wt. 218.25

Category : Sedative.

Dose : 0.4 to 1.2 g daily, in divided doses.

Description : White, crystalline powder; odour, characteristic; taste, slightly bitter.

Solubility : Slightly soluble in *water*; freely soluble in *acetone* and in *alcohol*; sparingly soluble in *solvent ether*.

Standards : Meprobamate is 2-methyl-2-propyltrimethylene dicarbamate. It contains not less than 97.0 per cent and not more than the equivalent of 101.0 per cent of $C_9H_{18}N_2O_4$, calculated with reference to the dried substance.

Identification : (A) To 0.5 g add 1 ml of *acetic anhydride* and 1 drop of *sulphuric acid* and shake well to effect solution. Set aside for thirty minutes after effecting solution. Pour the solution in 50 ml of *water*, while stirring the mixture vigorously, and allow to crystallise. Filter off the crystals, wash with *water* until the odour of acetic acid is no longer perceptible, and dry in vacuum at 60° for one hour; melting range of the crystals is between 124° to 130°, Appendix 5.11.

(B) Dissolve 20 mg in 2 ml of a 1 per cent w/v solution of *dimethylaminobenzaldehyde* in *sulphuric acid*; a yellow colour is produced which changes to orange after a few minutes. Heat on a water-bath for two minutes; the colour changes to red. Allow to cool and add, dropwise, 5 ml of *water*; the colour changes first to dark red and then to blue-violet.

(C) Dissolve 0.2 g in 15 ml of *0.5N alcoholic potassium hydroxide* and heat under a reflux condenser for fifteen minutes. Add 0.5 ml of *glacial acetic acid* and 1 ml of a 5 per cent w/v solution of *cobalt nitrate* in *ethyl alcohol*; an intense blue colour develops.

Melting range : Between 103° and 107°, Appendix 5.11.

Heavy metals : Not more than 20 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

Related impurities : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G*

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

as the coating substance and a mixture of 50 volumes of *acetone* and 50 volumes of *toluene* as the mobile phase. Apply separately to the plate 5 µl of each of two solutions in *alcohol* containing (1) 4.0 per cent w/v substance being examined and (2) 0.04 per cent w/v of the substance being examined. After removal of the plate dry it for ten minutes at 120°, cool, spray with a solution of 0.25 g of *vanillin* in a cooled mixture of 40 ml of *sulphuric acid* and 10 ml of *alcohol* and heat for fifteen minutes at 120°. Any spot in the chromatogram other than the principal spot obtained with solution (1) is not more intense than the spot obtained with solution (2).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying "in vacuo at 60°" for three hours, Appendix 5.8.

Assay : To 0.3 g add 25 ml of a 25 per cent v/v solution of *sulphuric acid* and boil under a reflux condenser for three hours. Cool, add an excess of *5N sodium hydroxide*, distil the liberated ammonia into 50 ml of *0.1N sulphuric acid* and titrate the excess of acid with *0.1N sodium hydroxide*, using *methyl red solution* as indicator. Repeat the operation without the substance being examined; the difference between the titration represents the amount of sulphuric acid required. Each ml of *0.1N sulphuric acid* is equivalent to 0.01091g of $C_9H_{18}N_2O_4$.

Storage : Store in tightly-closed containers.

Meprobamate Tablets

Category : Sedative.

Dose : Meprobamate, 0.4 to 1.2 g daily.

Usual strengths : 0.2 g; 0.4 g.

Standards : Meprobamate Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Meprobamate, $C_9H_{18}N_2O_4$.

Identification : To a quantity of the finely powdered tablets equivalent to 0.8 g of Meprobamate, add 5 ml of *chloroform*, heat to boiling, filter the hot mixture into 10 ml of *solvent hexane* and mix the liquids. Filter off the crystals formed with the aid of suction, and dry at 60°; the crystals melt between 103° and 107°, Appendix 5.11.

Related impurities : Comply with the test described under Meprobamate, applying to the plate 5 µl of each of the following solutions: For solution (1) extract a quantity of the powdered tablets equivalent to 0.4 g of Meprobamate with 5 ml of *alcohol*, centrifuge, and use the supernatant liquid. For solution (2) dilute 1 volume of solution (1) to 100 volumes with *alcohol*.

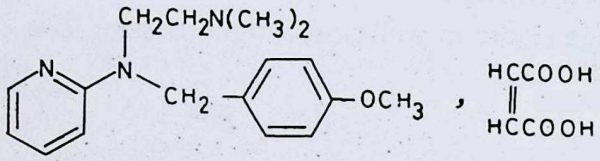
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 0.3 g of Meprobamate, add 100 ml of *5N hydrochloric acid* and boil under a reflux condenser for one hour. Complete the **Assay** described under Meprobamate, beginning at the words "Cool, add an excess of *5N sodium hydroxide*.....".

Storage : Store in well-closed containers.

Mepyramine Maleate

Pyrilamine Maleate



$C_{17}H_{23}N_3O,C_4H_4O_4$ Mol. Wt. 401.46

Category : Antihistaminic (H_1-receptor antagonist).

Dose : 0.3 to 0.6 g daily, in divided doses.

By intramuscular or intravenous injection, 25 to 50 mg.

Description : White or creamy-white powder; odour, slight; taste, bitter.

Solubility : Very soluble in *water*, freely soluble in *alcohol* and in *chloroform*.

Standards : Mepyramine Maleate is the maleate of 2-(*N*-*p*-anisyl-*N*-2-pyridylamino) ethyldimethylamine. It contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of $C_{17}H_{23}N_3O$, $C_4H_4O_4$, calculated with reference to the dried substance.

Identification : (A) Dissolve 0.2 g in 3 ml of *water*, add 3 ml of *sodium hydroxide solution* and shake with three successive quantities each of 3 ml, of *solvent ether*. To the aqueous layer add 2 ml of *bromine solution*, warm in a water-bath for ten minutes heat to boiling, cool and add a few drops to a solution of 10 mg of *resorcinol* in 3 ml of *sulphuric acid*, and heat on a water-bath for fifteen minutes; a blue-black colour is produced.

(B) To 2 ml of a 1 per cet w/v solution, add 1 ml of *cyanogen bromide solution* and 5 ml of a 2 per cent w/v solution of *potassium hydrogen phthalate*, mix and set aside for fifteen minutes, add 1 ml of a 4 per cent w/v solution of *aniline* in *alcohol*; a yellow colour is produced.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

(C) Dissolve about 0.5 g in 5 ml of *water* add 2 ml of *sodium hydroxide solution*; extract by shaking with two quantities, each of 5 ml, of *solvent ether*; wash the combined ether extracts with 3 ml of *water*; evaporate to dryness; dissolve the residue in 5 ml of *methyl alcohol* and pour into a solution of 0.5 g of *picric acid* in 5 ml of *methyl alcohol*; filter; the precipitate after washing with *methyl alcohol*, recrystallising from *methyl alcohol* and drying at 105°, melts at about 163°, Appendix 5.11.

(D) The light absorption, in the range 220 to 350 nm, of a 1-cm layer of a 0.001 per cent w/v solution in *0.01N hydrochloric acid* exhibits two maxima, at 239 nm and 316 nm; *extinction* at 239 nm, about 0.45 and at 316 nm, about 0.205, Appendix 5.15 A.

Melting range : Between 98° to 101°, Appendix 5.11.

pH : Between 4.7 to 5.2 determined in 1.0 per cent w/v solution, Appendix 5.10.

Arsenic : Not more than 2 parts per million, Appendix 3.2.1.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel GF 254* as the coating substance and a mixture of 5 volumes of *ethyl acetate*, 3 volumes of *methyl alcohol* and 2 volumes of *dilute acetic acid* as the mobile phase. Apply separately to the plate 10 µl of each of the following two solutions: For solution (1) dissolve 50 mg in 5 ml of *water*, add 2 ml of *dilute sodium hydroxide solution* and extract with two quantities, each of 20 ml, of *chloroform*. Shake the combined extracts with 5 g of *anhydrous sodium sulphate*, filter, evaporate to dryness using a rotary film evaporator and dissolve the residue in 2.5 ml of *chloroform*. For solution (2) dilute 1 volume of solution (1) to 500 volumes with *chloroform*. After removal of the plate, allow it to dry in air and examine under an ultraviolet lamp having a maximum output at about 254 nm. Spray the plate with *potassium iodoplatinate solution*. Any spot in the chromatogram obtained with solution (1), other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (2).

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 80°, Appendix 5.8.

Assay : Weigh accurately about 0.5 g and dissolve in 20 ml of *glacial acetic acid*. Add 2 drops of *crystal-violet solution* and titrate with *0.1N perchloric acid* to a blue-green end-point. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02007 g of $C_{17}H_{23}N_3O,C_4H_4O_4$.

Storage : Store in well-closed containers.

Mepyramine Tablets

Mepyramine Maleate Tablets; Pyrilamine Maleate Tablets

Category : Antihistaminic(H_1-receptor-antagonist).

Dose : Mepyramine Maleate, 0.3 to 0.6 g daily, in divided doses.

Usual strength : 50 mg.

Standards : Mepyramine Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Mepyramine Maleate, $C_{17}H_{23}N_3O, C_4H_4O_4$. The tablets may be coated.

Identification : The powdered tablets, freed as far as possible from coating, comply with the **Identification** tests (A) to (C) described under Mepyramine Maleate.

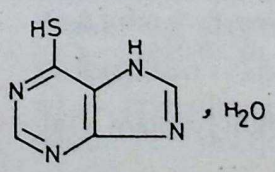
Related substances : Comply with the test described under Mepyramine Maleate using as solution (1) a solution prepared in the following manner: Shake a quantity of the powdered tablets equivalent to 50 mg of Mepyramine Maleate with 10 ml of *water* for two minutes. Add 2 ml of *N sodium hydroxide* and extract with two quantities, each of 20 ml, of *chloroform*. Shake the combined extracts with 5 g of *anhydrous sodium sulphate*, filter, evaporate to dryness in a current of air, and dissolve the residue in 2.5 ml of *chloroform*.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 0.1 g of Mepyramine Maleate, add 75 ml of *water* and 5 ml of *dilute hydrochloric acid*, shake vigorously for ten minutes, and add sufficient *water* to produce 100.0 ml. Centrifuge and dilute 10.0 ml of the clear supernatant liquid to 100.0 ml with *water*. To 10.0 ml add 10 ml of *0.1N hydrochloric acid* and sufficient *water* to produce 100.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 316 nm, Appendix 5.15 A. Calculate the content of $C_{17}H_{23}N_3O, C_4H_4O_4$, taking 206 as the value of E(1 per cent, 1-cm) at the maximum at about 316 nm.

Storage : Store in tightly-closed containers.

Mercaptopurine



$C_5H_4N_4S,H_2O$ Mol. Wt. 170.19

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Category : Antineoplastic.

Dose : 0.1 to 0.2 g daily, in divided doses.

Description : Yellow, crystalline powder, odourless; almost tasteless.

Solubility : Insoluble in *water*, in *acetone* and in *solvent ether*; soluble in hot *alcohol* and in solutions of alkali hydroxides, slightly soluble in *dilute sulphuric acid.*

Standards : Mercaptopurine is the monohydrate of purine-6-thiol. It contains not less than 97.0 per cent and not more than the equivalent of 102.0 per cent of $C_5H_4N_4S$ calculated with reference to the anhydrous substance.

Identification : (A) Dissolve 50 mg in 5 ml of *dimethyl sulphoxide* and add sufficient *0.1N hydrochloric acid* to produce 500 ml; dilute 25 ml to 1000 ml with *0.1N hydrochloric acid.* The light absorption of the resulting solution, in the range 230 to 350 nm, exhibits a maximum only at 325 nm, Appendix 5.15 A.

(B) Dissolve 20 mg in 20 ml of warm *alcohol* and add 1 ml of a saturated solution of *mercuric acetate* in *alcohol*; a white precipitate is produced.

(C) Dissolve 20 mg in 20 ml of warm *alcohol* and add 1 ml of a 1 per cent w/v solution of *lead acetate* in *alcohol*; a yellow precipitate is produced.

Hypoxanthine : Dissolve 50 mg in 5 ml of *dimethyl sulphoxide* and add sufficient *0.1N hydrochloric acid* to produce 500 ml. Dilute 25 ml to 1000 ml with *0.1N hydrochloric acid* and measure the *extinction* of a 1-cm layer of the resulting solution at 325 nm. Dilute a further 50 ml of the original solution to 100 ml with *0.1N hydrochloric acid* and measure the *extinction* of a 1-cm layer of the resulting solution at 255 nm; ratio of the *extinction* at 255 nm to that at 325 nm, not greater than 1.05, Appendix 5.15 A.

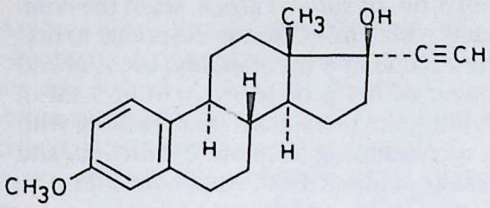
Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Water : Not less than 10.0 per cent and not more than 12.0 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately about 0.3 g and dissolve in 80 ml of *dimethylformamide.* Add 5 drops of a 1.0 per cent w/v solution of *thymol blue* in *dimethylformamide*, and titrate with *0.1N sodium methoxide*, using a magnetic stirrer and taking precautions against absorption of atmospheric carbon dioxide. Perform a blank determination, and make any necessary correction. Each ml of *0.1N sodium methoxide* is equivalent to 0.01522 g of $C_5H_4N_4S$.

Storage : Store is well-closed light-resistant containers.

Mestranol



$C_{21}H_{26}O_2$ Mol. Wt. 310.44

Category : Estrogen.

Dose : 0.05 to 0.15 mg daily, usually in conjunction with a progestogen.

Description : White or almost white, crystalline powder; odourless.

Solubility : Insoluble in *water*; freely soluble in *chloroform*; sparingly soluble in *ethyl alcohol*; slightly soluble in *methyl alcohol.*

Standards : Mestranol is 3-methoxy-19-nor-17α-pregna-1,3,5(10)-trien-20-yn-17β-ol. It contains not less than 97.0 per cent and not more than the equivalent of 102.0 per cent of $C_{21}H_{26}O_2$, calculated with reference to the dried substance.

Identification : (A) Complies with the test for *identification of steroids*, Appendix 3.3.11, using *solvent II* and *mobile phase D.*

(B) Dissolve 2 mg in 2 ml of *sulphuric acid*; the solution turns orange-red in colour, shows a yellowish-green fluorescence by transmitted light and complies with the following tests:

(a) To 1 ml add one drop of *ferric ammonium sulphate solution* and 2 ml of *water*; a reddish-brown flocculent precipitate is produced.

(b) To 1 ml add 2 ml of *water*; a rose-red flocculent precipitate is produced.

(c) Insoluble in a 5 per cent w/v solution of *potassium hydroxide.*

Melting range : Between 146° and 154°, Appendix 5.11.

Specific optical rotation : between +2° and +8°, calculated with reference to the dried substance and determined in a 1.0 per cent w/v solution in *dioxan*, Appendix 5.12.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.2 g, dissolve in 40 ml of *tetrahydrofuran*, add 10 ml of a 10 per cent w/v solution of *silver nitrate* and titrate with *0.1N sodium hydroxide*, determining the end-point potentiometrically. Perform a

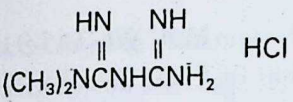
CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

blank determination and make any necessary correction. Each ml of *0.1N sodium hydroxide* is equivalent to 0.03104 g of $C_{21}H_{26}O_2$.

Storage : Store in well-closed light-resistant containers.

Metformin Hydrochloride



$C_4H_{11}N_5, HCl$ Mol. Wt: 165.62

Category : Oral hypoglycaemic.

Dose : 0.5 to 2.0 g daily, in divided doses.

Description : White, crystalline powder; almost odourless; hygroscopic.

Solubility : Freely soluble in *water*; sparingly soluble in *alcohol*; practically insoluble in *chloroform* and in *solvent ether*.

Standards : Metformin is the hydrochloride of 1,1-dimethylbiguanide. It contains not less than 98.5 per cent and not more than the equivalent of 101.0 per cent of $C_4H_{11}N_5, HCl$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *metformin hydrochloride R.S.*, Appendix 5.15 B.

(B) Dissolve 25 mg in 5 ml of *water*, add 1.5 ml of *5N sodium hydroxide*, 1 ml of *α-naphthol solution* and, dropwise with shaking, 0.5 ml of *dilute sodium hypochlorite solution*; an orange-red colour is produced which darkens on keeping.

(C) Dissolve 10 mg in 10 ml of *water* and add 10 ml of a solution prepared by mixing equal volumes of a 10 per cent w/v solution of *sodium nitroprusside*, a 10 per cent w/v solution of *potassium ferricyanide* and a 10 per cent w/v solution of *sodium hydroxide* and allowing to stand for twenty minutes; a wine-red colour develops within three minutes.

(D) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

(E) It melts at about 225°, Appendix 5.11.

Dicyandiamide : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using as the coating substance a suitable cellulose powder, and heating the coated plate at 105° for ten minutes. The mobile phase is a mixture of 6 volumes of *isobutyl methyl ketone*, 4 volumes of *methoxyethanol*, 0.6 volumes of *glacial acetic acid*, and 1 volume of *water*. Dissove 0.5 g of the substance being examined, in 5 ml of hot *methyl alcohol*, cool to 30°, add with stirring, 5 ml of *solvent ether*, cool to 20°, and allow to stand for thirty minutes; filter through a sintered-glass crucible, wash with 2.5 ml of *solvent ether*, and evaporate the combined filtrate and washings to dryness on a water-bath. Apply separately to the plate 10 µl of each of the following solutions: For solution (1) dissolve the residue obtained above in 0.5 ml of *water*; solution (2) is a 0.04 per cent w/v solution of *dicyandiamide*. After removal of the plate, dry it at 105° for ten minutes, and spray with a solution prepared by mixing equal volumes of a 10 per cent w/v solution of *sodium nitroprusside*, a 10 per cent w/v solution of *potassium ferricyanide* and a 10 per cent w/v solution of *sodium hydroxide*, and allowing to stand for twenty minutes. The spot in the chromatogram obtained with solution (2) is more intense than any corresponding spot in the chromatogram obtained with solution (1).

Heavy metals : Not more than 20 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

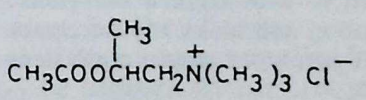
Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.25 g, dissolve in 50 ml of *glacial acetic acid*, add 10 ml of *mercuric acetate solution*—and titrate with *0.1N perchloric acid*, determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.008281 g of $C_4H_{11}N_5, HCl$.

Storage : Store in tightly-closed containers.

Methacholine Chloride



$C_8H_{18}ClNO_2$ Mol. Wt. 195.69

Category : Cholinergic.

Dose : By subcutaneous injection; initial, 10 mg; then 25 mg may be given 10 to 30 minutes later.

Description : Colourless or white crystals, or white, crystalline powder; odourless or with slight odour. Very deliquescent.

Solubility : Very soluble in *water*; freely soluble in *alcohol* and in *chloroform*.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Standards : Methacholine Chloride is 2-acetoxypropyl trimethylammonium chloride. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_8H_{18}ClNO_2$, calculated with reference to the dried substance.

Identification : (A) To about 0.1 g on a watch glass add 3 ml of *platinic chloride solution* previously diluted with 2 ml of *water*; small rhombohedric plates are formed (difference from acetylcholine chloride which forms needles radiating from a central point, and from choline chloride which forms no crystals).

(B) To 1 ml of a 10 per cent w/v solution add 1 ml of *alcohol* and 1 ml of *sulphuric acid* and heat gently; ethyl acetate is produced.

(C) To 5 ml of 10 per cent w/v solution add 2 g of *potassium hydroxide* and heat gently; the odour of trimethylamine is perceptible.

(D) A solution (1 in 50) gives the reactions of *chlorides*, Appendix 3.1.

Melting range : Between 170° and 173°, Appendix 5.11.

pH : Between 4.5 and 5.5, determined in a 2.0 per cent w/v solution, Appendix 5.10.

Acetylcholine chloride : To 2 ml of a 10 per cent w/v solution add a solution prepared by neutralising 0.5 ml of *perchloric acid (60 per cent)* to *litmus paper* with *sodium hydroxide solution*, and adding sufficient *water* to produce 3 ml, shake well and cool in ice for five minutes; no precipitate is produced.

Heavy metals : Not more than 20 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

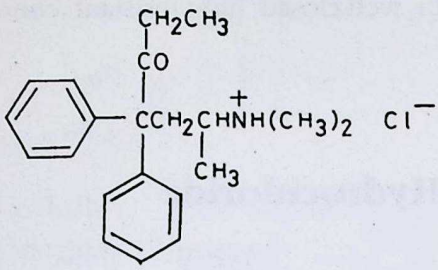
Loss on drying : Not more than 1.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.4 g, previously dried and stored in a vacuum desiccator, and dissolve in 50 ml of *glacial acetic acid*; add 10 ml of *mercuric acetate solution*, one drop of *crystal-violet solution* and titrate with *0.1N perchloric acid* to a blue-green end-point. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.01957 g of $C_8H_{18}ClNO_2$.

Storage : Store in tightly-closed containers.

Methadone Hydrochloride

Amidone Hydrochloride



$C_{21}H_{28}ClNO$ Mol. Wt. 345.91

Category : Narcotic analgesic; narcotic abstinence syndrome suppressant.

Dose : Oral, 5 to 10 mg. By subcutaneous injection, 5 to 10 mg.

Description : Colourless crystals or white, crystalline powder; almost odourless; taste, bitter.

Solubility : Soluble in *water*; freely soluble in *alcohol*, and in *chloroform*; practically insoluble in *solvent ether*.

Standards : Methadone Hydrochloride is N, N-dimethyl(1-methyl-4-oxo-3,3-diphenylhexyl) ammonium chloride. It contains not less than 98.5 per cent and not more than the equivalent of 100.5 per cent of $C_{21}H_{28}ClNO$, calculated with reference to the dried substance.

Identification : (A) Place a few crystals in a white porcelain crucible and add 1 drop of a 2 per cent w/v solution of *nitrobenzene*, stir and add 1 drop of a 50 per cent w/v solution of *sodium hydroxide*; a purple colour which changes to dark brown is produced.

(B) Dissolve 0.1 g in 10 ml of *water*, add 0.125 g of *picrolonic acid* dissolved in 50 ml of boiling *water*, stir, and set aside for two hours; melting range of the residue, after recrystallisation, and washing with *alcohol (20 per cent)*, and drying at 105°, is about 160° or about 180°, Appendix 5.11.

(C) Dissolve about 10 mg in 2 ml of *water*, and add 2 ml of *methyl orange solution*; a yellow precipitate is formed.

(D) A solution (1 in 20) gives the reaction of *chlorides*, Appendix 3.1.

Melting range : Between 233° and 236°, Appendix 5.11.

pH : Between 4.5 to 6.5, determined in a 1.0 per cent w/v solution, Appendix 5.10.

Clarity and colour of solution : A 2.5 per cent w/v solution is clear and colourless.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G*

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

as the coating substance and a mixture of 6 volumes of *alcohol*, 3 volumes of *glacial acetic acid* and 1 volume of *water* as the mobile phase. Apply separately to the plate 5 µl of each of two solutions in *alcohol* containing (1) 10 per cent w/v of the substance being examined and (2) 0.01 per cent w/v of the substance being examined. After removal of the plate allow it to dry in air and spray with *dilute potassium iodobismuthate solution*. Any spot in the chromatogram obtained with solution (1), other than the principal sopt, is not more intense than the spot in the chromatogram obtained with solution (2).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.5 g and dissolve in a mixture of 10 ml of *glacial acetic acid* and 10 ml of *mercuric acetate solution*, warming slightly if necessary to effect solution. Cool, add 10 ml of *dioxan*, ten drops of *crystal violet solution*, and titrate rapidly with *0.1N perchloric acid*. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.03459 g of $C_{21}H_{28}ClNO$.

Storage : Store in tightly-closed containers.

Methadone Injection

Methadone Hydrochloride Injection, Amidone Hydrochloride Injection

Category : Narcotic analgesic; narcotic abstinence syndrome suppressant.

Dose : Methadone Hydrochloride. By subcutaneous injection, 5 to 10 mg.

Usual strengths : 5 mg in 1 ml; 10 mg in 1 ml.

Standards : Methadone Injection is a sterile solution of Methadone Hydrochloride in Water for Injection. It contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Methadone Hydrochloride, $C_{21}H_{27}NO, HCl$.

Identification : Complies with **Identification** test (B) and (D) described under Methadone Hydrochloride.

pH : Between 5.0 and 6.5, Appendix 5.10.

Other requirements : Complies with the requirements stated under Injections.

Assay : Dilute an accurately measured volume equivalent to about 0.1 g of Methadone Hydrochloride to 20 ml with *water* and carry out the **Assay** described under Methadone tablets, beginning at the words "make alkaline to *litmus solution*.....".

Storage : Store in single-dose or multiple-dose, light-resistant containers.

Methadone Tablets

Amidone Hydrochloride Tablets, Methadone Hydrochloride Tablets

Category : Narcotic analgesic; narcotic abstinence syndrome suppressant.

Dose : Methadone Hydrochloride, 5 to 10 mg.

Usual strengths : 5 mg and 10 mg.

Standards : Methadone Tablets contain not less than 93.0 per cent and not more than 107.0 per cent of the stated amount of Methadone Hydrochloride, $C_{21}H_{27}NO, HCl$.

Identification : Triturate a quantity of the finely powdered tablets equivalent to about 0.2 g of Methadone Hydrochloride with, 15 ml of warm *alcohol* for twenty minutes, filter and evaporate the filtrate on a water-bath to dryness; the residue complies with **Identification** tests (A) and (D) described under Methadone Hydrochloride.

Uniformity of content : Crush one tablet to a fine powder and transfer to a 25 ml volumetric flask. Add 20 ml of *water*, mix by shaking and make up to volume with *water*. Mix well and centrifuge. Dilute a suitable volume of the clear, supernatant liquid with *water* to produce a solution containing about 0.2 mg of Methadone Hydrochloride per ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 291 nm, Appendix 5.15 A. Calculate the content of $C_{21}H_{27}ClNO, HCl$ from the *extinction* obtained by repeating the determination on an accurately weighed quantity of *methadone hydrochloride R.S.* in place of the substance being examined.

Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 90 per cent and 110 per cent of the average except that for one tablet the content may be between 85 per cent and 115 per cent of the average.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh 20 tablets or more if necessary, and reduce to fine powder. Weigh accurately a quantity of the powder equivalent to about 0.1 g of Methadone Hydrochloride, transfer to a separating funnel containing 20 ml of *water*, make alkaline to *litmus solution* by the addition of *sodium hydroxide solution* and extract with four successive quantities of 50, 25, 25 and 10 ml of *solvent ether*. Wash the combined ether extracts with two

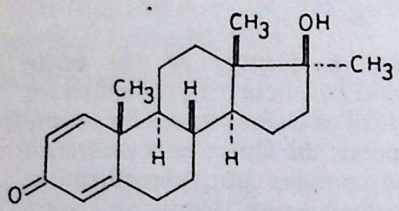
CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

quantities, each of 10 ml of a mixture of equal parts of *water* and *sodium chloride solution*. Extract the combined washings with 10 ml of *solvent ether* and add the ether to the combined ether extracts. Shake the ether solution with 20.0 ml of *0.02N hydrochloric acid*, allow to separate and transfer the acid layer to a flask. Repeat the extraction with two quantities, each of 10 ml of *water*, add the aqueous extracts to the acid layer, warm the flask on water-bath to remove the ether, and titrate the excess of acid with *0.02N sodium hydroxide*, using *methyl red solution* as indicator. Each ml of *0.02N hydrochloric acid* is equivalent to 0.006918 g of $C_{21}H_{27}NO,HCl$.

Storage : Store in well-closed, light-resistant containers.

Methandienone



$C_{20}H_{28}O_2$ Mol. Wt. 300.42

Category : Anabolic steroid, weak androgen.

Dose : Adults, 5 to 10 mg, daily; Children, 0.5 to 1 mg daily.

Description : White or faintly yellowish-white, crystalline powder, odourless.

Solubility : Insoluble in *water*; soluble in *alcohol*, in *chloroform*, and in *glacial acetic acid*; slightly soluble in *solvent ether*.

Standards : Methandienone is 17β-hydroxy-17α-methyl-1,4-androstadien-3-one. It contains not less than 97.0 per cent and not more than the equivalent of 103.0 per cent of $C_{20}H_{28}O_2$, calculated with reference to the dried substance.

Identification : (A) Dissolve 50 mg in 9 ml of *methyl alcohol* in a test-tube, add 1 ml of *dinitrophenlhydrazine solution*, and scratch the inside of the test-tube to induce crystallisation. The precipitate, after washing with *water*, melts at about 213°, Appendix 5.11.

(B) Dissolve 10 mg in *nitrobenzene*, add 0.5 g of *anhydrous aluminium chloride*, and shake for several minutes; a red colour is produced.

(C) *The infra-red absorption spectrum* exibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *methandienone R.S.*, Appendix 5.15B.

Melting range : Between 163° and 167°, Appendix 5.11.

Specific optical rotation : Between +8° and +14°, determined in a 1 per cent w/v solution in *alcohol*, Appendix 5.12.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of equal volumes of *cyclohexane* and *ethyl acetate* as the mobile phase. Apply separately to the plate 2 µl of each of four solutions in *alcohol* containing (1) 5.0 per cent w/v of the substance being examined, (2) 0.025 per cent w/v of *methyltestosterone R.S.*, (3) 0.1 per cent w/v of *6α-hydroxymethandienone R.S.*, and (4) 0.1 per cent w/v of *6β-hydroxymethandienone R.S.* After removal of the plate, allow it to dry in air for ten minutes, spray with a 0.5 per cent w/v solution of *vanillin* in a mixture of 4 volumes of *sulphuric acid* and 1 volume of *alcohol* and heat at 105° for five minutes. Any spots in the chromatogram obtained with solution (1), other than the principal spot, are not more intense than the corresponding spots in the chromatograms obtained with solutions (2), (3) and (4).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying "in vacuo at 100°", Appendix 5.8.

Assay : Dissolve 50 mg in sufficient *ethyl alcohol* to produce 500.0 ml, dilute 10.0 ml to 100.0 ml with *ethyl alcohol* and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 245 nm, Appendix 5.15A. Calculate the content of $C_{20}H_{28}O_2$, taking 516 as the value of E(1 per cent, 1-cm) at the maximum at about 245 nm.

Storage : Store in well-closed, light-resistant containers.

Methandienone Tablets

Category : Anabolic steroid, weak androgen.

Dose : Methandienone. Adults, 5 to 10 mg daily; Children, 0.5 to 1 mg daily.

Usual strength : 5 mg.

Standards : Methandienone Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Methandienone, $C_{20}H_{28}O_2$.

Identification : Heat the powdered tablets for ten minutes with *solvent ether* under a reflux condenser, filter and remove the ether from the extract. The residue

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

complies with the **Identification** tests described under Methandienone.

Uniformity of content : Powder one tablet, add sufficient *chloroform* to produce 50.0 ml, shake for twenty minutes, allow to settle, and centrifuge in a stoppered tube. Carry out the **Assay** beginning at the words "Evaporate 5 ml of the supernatant liquid....".

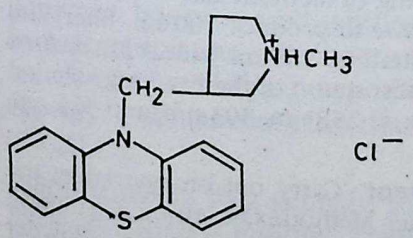
Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 90 and 110 per cent of the average except that for one tablet the content may be between 85 and 115 per cent of the average.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 5 mg of Methandienone, add sufficient *chloroform* to produce 50 ml, shake for twenty minutes, allow to settle, and centrifuge in a stoppered tube. Evaporate 5 ml of the supernatant liquid to dryness, dissolve the residue in 2 ml of *aldehyde-free alcohol*, add 10 ml of a hot, freshly prepared and filtered 0.25 per cent w/v solution of *dinitrophenylhydrazine* in *2N hydrochloric acid*, mix gently, and heat on a water-bath for thirty minutes, with precautions against loss of liquid by evaporation. Cool, allow to stand overnight, filter through a sintered-glass filter (grade 4, maximum pore size 5 to 15 μm), wash the precipitate in succession with 50 ml of *2N hydrochloric acid* and 50 ml of *water*, dry at 105° for thirty minutes, and dissolve in sufficient *chloroform* to produce 100.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 402 nm, Appendix 5.15 A, using as the blank a solution obtained by treating 2 ml of *aldehyde-free alcohol* in the same way, beginning at the words "add 10 ml.....". Calculate the content of $C_{20}H_{28}O_2$ from the *extinction* obtained by repeating the operation using a suitable quantity of *methandienone R.S.*

Storage : store in tightly-closed, light-resistant containers.

Methdilazine Hydrochloride



$C_{18}H_{20}N_2S,HCl$ Mol. Wt. 332.89

Category : Antipruritic.

Dose : 8 mg, two to four times daily.

Description : Light tan powder, turning pale-pink to brown on exposure to light; odour slight; and characteristic.

Solubility : Freely soluble in *water*, in *alcohol* and in *chloroform*.

Standards : Methdilazine Hydrochloride is 3-(phenothiazin-10-yl)methyl-1-methylpyrrolidinium chloride. It contains not less than 97.0 per cent and not more than the equivalent of 103.0 per cent of $C_{18}H_{20}N_2S,HCl$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *methdilazine hydrochloride R.S*, Appendix 5.15 B.

(B) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.0005 per cent w/v solution exhibits a maximum at 252 nm and an inflection at 275 nm; *extinction* at 252 nm, about 0.46, Appendix 5.15 A.

(C) Dissolve 50 mg in *dilute hydrochloric acid*. Add 3 ml of *buffered palladium chloride solution* and 1 ml 1 per cent w/v solution of *sodium lauryl sulphate* and mix; a dark blue colour is formed.

(D) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

Melting range : Between 184° and 190°, Appendix 5.11.

pH : Between 4.8 and 6.0, determined in a 1.0 per cent w/v solution, Appendix 5.10.

Heavy metals : Not more than 20 parts per million, determined by Method B, Appendix 3.2.4.

Sulphated ash : Not more than 0.5 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1 g by drying "in vacuo at 65°" for 16 hours, Appendix 5.8.

Assay : Weigh accurately about 0.1 g and dissolve in sufficient *water* to produce 100 ml. Transfer 5.0 ml of this solution to a 100-ml volumetric flask, dilute to volume with *water* and mix. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 252 nm and at 275 nm, Appendix 5.15 A. Subtract the *extinction* at 275 nm from the *extinction* at 252 nm. Calculate the content of $C_{18}H_{20}N_2S,HCl$ from the difference in the *extinction* obtained by carrying out the **Assay** simultaneously on *methdilazine hydrochloride R.S.*

Storage : Store in a tightly-closed, light-resistant container.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Methotrexate

$C_{20}H_{22}N_8O_5$ Mol. Wt. 454.4

Category : Antineoplastic; Antipsoriatic.

Dose : 5 to 100 mg at suitable intervals.

Description : Yellow to orange-brown, crystalline powder.

CAUTION – Great care should be taken to prevent inhaling particles of Methotrexate and exposing the skin to it.

Solubility : Practically insoluble in *water*, in *alcohol*, in *chloroform*, and in *solvent ether*; freely soluble in dilute solutions of alkali hydroxides and carbonates; slightly soluble in *dilute hydrochloric acid.*

Standards : Methotrexate is a mixture of 4-amino-10-methyl-folic acid and closely related compounds. It contains not less than 85 per cent of $C_{20}H_{22}N_8O_5$, calculated with reference to the anhydrous substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *methotrexate R.S.* Appendix 5.15 B.

(B) The light absorption, in the range 230 to 380 nm, of a 1-cm layer of a 0.001 per cent w/v solution in *0.1N sodium hydroxide* exhibits three maxima at 258 nm, 303 nm and 365 nm; *extinction* at 258 nm, about 0.5; at 303 nm, about 0.5 and at 365 nm about 0.2, Appendix 5.15 A.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Water : Not more than 8.0 per cent w/w, Appendix 3.3.25.

Assay : *NOTE – Throughout this procedure, exercise care to prevent exposure of Methotrexate and its solution to extremes of pH for significant lengths of time, and to prevent exposure to sunlight or heat above a temperature of 60°*

Prepare chromatograms by the method for *descending paper chromatography*, Appendix 5.4.2, using a freshly prepared 15.6 per cent w/v solution of *sodium dihydrogen phosphate* adjusted to pH 5.8 with *sodium hydroxide solution* as the mobile phase. Use four strips of paper 110 cm long and 4-cm wide. Draw five parallel lines across each strip, one at the centre, two on either side and 4 cm from the centre, and two on either side 6.5 cm from the centre. Apply at any three of the 6.5 cm lines 50 µl of a solution prepared by dissolving 60 mg of the methotrexate in sufficient of a 0.5 per cent w/v solution of *ammonium carbonate* to produce 50 ml; if necessary warm briefly at a temperature not exceeding 50 ° to effect solution (solution 1). Also apply at any other three of the 6.5-cm lines 50 µl of a solution prepared in the same manner using *methotrexate R.S.* (solution 2) and at the two remaining 6.5-cm lines, 50 µl of the 0.5 per cent w/v solution of *ammonium carbonate* (solution 3). Place a layer of *water* 2.5 cm deep in the bottom of the tank. Insert the strips of paper in such a manner that the centre lines lie under the glass rod in the solvent trough and the 4-cm lines lie along the tops of the guide-rods. Close the tank, allow to stand for sixteen hours, pour the mobile phase in the solvent trough, and elute until the solution nearly reaches the ends of the paper (about four hours). Examine the dry strips of paper under an ultra-violet lamp having a maximum output at about 254 nm and mark the methotrexate bands. Cut out the six methotrexate bands and the two corresponding portions from the strips carrying the ammonium carbonate solution. Treat each piece in the following manner: Cut into small pieces, place in a 50-ml glass-stoppered flask, shake vigorously with 25.0 ml of *0.1N hydrochloric acid* for thirty seconds, centrifuge, and measure the *extinction* of a 5-cm layer at the maximum at about 306 nm, using *0.1N hydrochloric acid* as the blank, Appendix 5.15 A. Calculate the weight of $C_{20}H_{22}N_8O_5$ in the weight of the methotrexate taken for the **Assay** from the expression $W(E_1\text{-}E_3)/(E_2\text{-}E_3)$, where W is the declared content of $C_{20}H_{22}N_8O_5$ in *methotrexate R.S.* and E_1, E_2 and E_3 are the means of the extinctions obtained from solution (1), solution (2), and solution (3) respectively.

Storage : Store in well-closed, light-resistant containers.

Methotrexate Tablets

Category : Antineoplastic; Antipsoriatic.

Dose : Methotrexate, 5 to 100 mg at suitable intervals.

Usual strength : 2.5 mg.

Standards : Methotrexate Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of, Methotrexate, $C_{20}H_{22}N_8O_5$.

Identification : Extract a quantity of the powdered tablets equivalent to 10 mg of Methotrexate with sufficient *0.1N sodium hydroxide* to produce 100 ml, filter, and dilute 10 ml of the filtrate to 100 ml with *0.1N sodium hydroxide*; the light absorption of the resulting solution exhibits three maxima, at 258 nm, 303 nm, and 365 nm, Appendix 5.15 A.

Uniformity of content : Carry out on one tablet the **Assay** described under Methotrexate, using as solution (1) a solution prepared in the following manner: Powder one tablet and shake with 5 ml of a 0.5 per cent w/v solution of *ammonium carbonate* for fifteen minutes, centrifuge, and use the supernatant liquid. For solution (2)

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

dissolve 25 mg of *methotrexate R.S.* in sufficient of a 0.5 per cent w/v solution of *ammonium carbonate* to produce 50 ml. Calculate the content of $C_{20}H_{22}N_8O_5$ in the tablet.

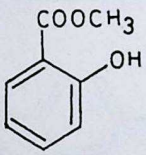
Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 90 and 110 per cent of the average except that for one tablet the content may be between 85 and 115 per cent of the average.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets or more if necessary. Carry out the **Assay** described under Methotrexate, using as solution (1) a solution prepared in the following manner: Weigh accurately a quantity of the powdered tablets equivalent to about 60 mg of Methotrexate and shake with 50 ml of a 0.5 per cent w/v solution of *ammonium carbonate* for fifteen minutes, centrifuge, and use the supernatant liquid.

Storage : Store in tightly-closed, light-resistant containers.

Methyl Salicylate



$C_8H_8O_3$ Mol. Wt. 152.15

Category : Counter-irritant; pharmaceutical aid (flavour).

Description : Colourless or pale yellow liquid; odour characteristic and aromatic; taste, sweet, warm and aromatic.

Solubility : Slightly soluble in *water*; freely soluble in *alcohol* and in *glacial acetic acid.*

Standards : Methyl Salicylate is methyl-o-hydroxybenzoate. It is produced synthetically or is obtained by maceration and subsequent with steam from the leaves of *Gaultheria procumbens* Linn. (Fam. Ericaceae). It contains not less than 99.0 per cent w/w of $C_8H_8O_3$.

Identification : To a saturated solution add a drop of *ferric chloride test-solution*; a violet colour is produced.

Refractive index : Between 1.5335 and 1.5345, Appendix 5.14.

Wt. per ml : Between 1.175 and 1.180 g (for natural material); 1.180 and 1.185 g (for synthetic material), Appendix 5.19.

Free acid : Shake 5.0 g with 25 ml of freshly boiled and cooled *water* for one minute, separate the aqueous layer, filter, and add 0.25 ml of *dilute phenolphthalein solution*; not more than 0.4 ml of *0.1N sodium hydroxide* is required to change the colour of the solution.

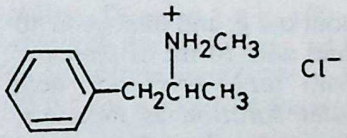
Assay : Weigh accurately about 0.5 g and dissolve in 25 ml of *alcohol.* Add 1 drop of *phenol red solution* and neutralise with *0.1N sodium hydroxide.* To the neutralised solution add 50.0 ml of *0.1N sodium hydroxide* and heat under reflux on a water-bath for 30 minutes. Cool and titrate with *0.1N hydrochloric acid.* Repeat the procedure without the substance being examined. Each ml of *0.1N sodium hydroxide* is equivalent to 0.01522 g of $C_8H_8O_3$.

Storage : Store in well-closed, light-resistant containers.

Labelling : The label on the container states whether it is made synthetically or distilled from plants.

Methylamphetamine Hydrochloride

Methamphetamine Hydrochloride



$C_{10}H_{15}N, HCl.$ Mol. Wt. 185.70

Category : Adrenergic, central stimulant.

Dose : 2.5 to 10 mg. By intramuscular or intravenous injection, 10 to 30 mg.

Description : Fine white crystals or white crystalline powder; odourless; taste bitter.

Solubility : Soluble in *water*, in *alcohol* and in *chloroform*; practically insoluble in *solvent ether.*

Standards : Methylamphetamine Hydrochloride is (*S*)(1-methyl-2-phenylethyl)methylammonium chloride. It contains not less than 98.0 per cent of $C_{10}H_{15}N, HCl$, calculated with reference to the dried substance.

Identification : (A) To 1 mg, add 3 drops of a mixture of 3 ml of *sulphuric acid* and 2 drops of *formaldehyde solution*; an intense brick-red colour immediately forms, which soon becomes brown and then slowly changes to dull olive-green.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

(B) To 1 g dissolved in 20 ml of *water*, add 10 ml of *sodium hydroxide solution* and 2 g of *dinitrobenzoyl chloride*. Shake for thirty minutes, filter and wash the residue with water until the washings are neutral to *phenolphthalein solution*. The residue after recrystallisation twice from *alcohol (60 per cent)* and drying "in vacuo" over phosphorus pentoxide, melts at about 115°, Appendix 5.11.

(C) Dissolve 2 mg in 1 ml of *N hydrochloric acid*, add 4 ml of *water*, 2 ml of *diazotised nitroaniline solution*, 4 ml of *N sodium hydroxide* and 2 ml of *n-butyl alcohol*, shake and allow to separate; no colour develops in the butyl alcohol layer (distinction from amphetamine).

(D) To 10 ml of a 1 per cent w/v solution add *mercuric chloride solution*; a crystalline precipitate is produced (distinction from phenylpherine and adrenaline).

(E) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

Melting range : Between 171° and 174°, Appendix 5.11.

Specific optical rotation : Between +16° and +18°, calculated with reference to the dried substance and determined in a 5 per cent w/v solution, Appendix 5.12.

Sulphate : 0.1 g complies with the *limit test for sulphates*, Appendix 3.2.8.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.4 g, and dissove in 30 ml of *glacial acetic acid*, and add 10 ml of *mercuric acetate solution*. Titrate with *0.1N perchloric acid* using 0.2 ml of *crystal-violet solution* as indicator, perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.01857 g of $C_{10}H_{15}N$, HCl.

Storage : Store in well-closed, light-resistant containers.

Methylamphetamine Injection

Methylamphetamine Hydrochloride Injection

Category : Adrenergic; central stimulant.

Dose : Methylamphetamine Hydrochloride, by intramuscular or intravenous injection, 10 to 30 mg.

Usual strength : 20 mg in 1 ml.

Standards : Methylamphetamine Injection is a sterile solution of Methylamphetamine Hydrochloride in Water for Injection. It contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of $C_{10}H_{15}N$, HCl.

Identification : (A) To a volume equivalent to 0.2 g of Methylamphetamine Hydrochloride, add 2 ml of *sodium hydroxide solution* and 0.4 g of *dinitrobenzoyl chloride*, shake for thirty minutes, filter and wash the residue with *water* until the washings are neutral to *phenolphthalein solution*. Rescrystallise the residue twice from *alcohol (60 per cent)* and dry in vacuum over phosphorus pentoxide. The residue melts at about 115°, Appendix 5.11.

(B) To a volume equivalent to 2 mg of Methylamphetamine Hydrochloride add 1 ml of *N hydrochloric acid*, 4 ml of *water*, 2 ml of *diazotised nitroaniline solution*, 4 ml of *N sodium hydroxide* and 2 ml of *n-butyl alcohol*, shake and allow to separate; no colour develops in the butyl alcohol layer (distinction from amphetamine).

(C) It gives the reactions of *chlorides*, Appendix 3.1.

Other requirements : Complies with the requirements stated under Injections.

Assay : Measure accurately a volume equivalent to about 0.1 g of Methylamphetamine Hydrochloride and dilute to 120 ml with *water*, add 2 ml of *sodium hydroxide solution*, and distil into 50.0 ml of *0.5N hydrochloric acid* until about 5 ml of liquid is left in the distillation flask. Titrate the excess of acid with *0.05N sodium hydroxide*, using *methyl red solution* as indicator. Each ml of *0.05N hydrochloric acid* is equivalent to 0.009285 g of $C_{10}H_{15}N$, HCl.

Storage : Store in single-dose or multiple-dose, light-resistant containers.

Industrial Methylated Spirit

I.M.S.

Category : Pharmaceutical aid (solvent).

Description : Colourless, clear, mobile and volatile liquid; odour, spirituous and of wood naphtha. It is readily volatilised even at low temperature, and boils at about 78°. It is inflammable.

Standards : Industrial Methylated Spirit is a mixture of 19 volumes of Alcohol with 1 volume of approved wood naphtha.

Identification : Mix 0.1 ml with 0.05 ml of a 11 per cent w/w solution of *phosphoric acid* and 0.25 ml of *potassium permanganate solution*. After one minute add a little *sodium metabisulphite* and shake until the mixture is decolorised. Add 1.5 ml of a 50 per cent v/v solution of *sulphuric acid* and a little finely-powdered *chyomotropic acid*. Shake well and heat on a water-bath for five minutes; a deep violet colour is produced.

Acidity or Alkalinity : 25 ml requires not more than 0.2 ml of *0.1N sodium hydroxide* to give a pink colour with

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

phenolphthalein solution, and not more than 1.0 ml of *0.1N hydrochloric acid* to give a red colour with *methyl red solution*.

Specific gravity : Not greater than 0.815, Appendix 5.19.

Clarity of solution : Dilute 5 ml to 100 ml with *water*; the solution is clear.

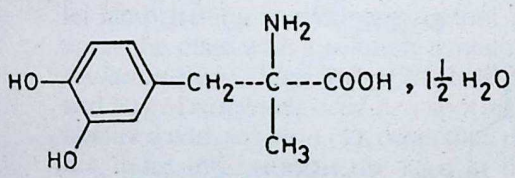
Aldehydes : Not more than 50 parts per million, determined by the following method: To 5.0 ml add 5 ml of *water* and 1 ml of *decolorised magenta solution* and allow to stand for thirty minutes; any colour produced is not more intense than that obtained by similarly treating 2.5 ml of a 0.01 per cent w/v solution of *acetaldehyde* in *aldehyde-free alcohol* diluted to 5 ml with the same solvent.

Non-volatile matter : Not more than 0.01 per cent w/v, determined by evaporating 100 ml and drying the residue at 105°.

Storage : Store in tightly-closed, containers, away from fire.

Labelling : The label on the container states "Inflammable"

Methyldopa



$C_{10}H_{13}NO_4.1\frac{1}{2}H_2O$ Mol. Wt. 238.24

Category : Antihypertensive.

Dose : The equivalent of 0.5 to 3 g of anhydrous methyldopa, daily, in divided doses.

Description : White to yellowish-white, fine powder which may contain friable lumps; odourless; almost tasteless.

Solubility : Sparingly soluble in *water*, slightly soluble in *alcohol*, practically insoluble in *solvent ether*, very soluble in *dilute hydrochloric acid*.

Standards : Methyldopa in the sesquihydrate of 3-(3,4-dihydroxyphenyl)-2-methyl-L-alanine. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_{10}H_{13}NO_4$, calculated with reference to the anhydrous substance.

Identification : (A) To 10 mg add 3 drops of a 0.4 per cent w/v solution of *ninhydrin* in *sulphuric acid*; a dark purple colour is produced within five to ten minutes. Add 3 drops of *water*; the colour changes to pale brownish-yellow.

(B) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *microcrystalline cellulose* as the coating substance (Merck microcrystalline cellulose is suitable) and a mixture of 50 volumes of *n-butyl alcohol*, 25 volumes of *glacial acetic acid* and 25 volumes of *water* as the mobile phase. Apply separately to the plate 5 µl of each of two solutions in *N hydrochloric acid* containing (1) 1 per cent w/v of the substance being examined and (2) 1 per cent w/v of *methyldopa R.S.* After removal of the plate, dry it in a current of warm air, and spray with a solution freshly prepared by mixing equal volumes of a 10 per cent w/v solution of *ferric chloride* and a 5 per cent w/v solution of *potassium ferricyanide*. The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

(C) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.004 per cent w/v solution in *0.1N hydrochloric acid* exhibits a maximum only at 280 nm; *extinction* at 280 nm, about 0.46, Appendix 5.15 A.

Optical rotation : Between −1.10° and −1.23°, determined in a solution prepared by dissolving a quantity equivalent to 2.2 g of the dried substance in 25 ml of *aluminium chloride solution* and diluting to 50.0 ml with *water*, Appendix 5.12.

Acidity : Dissolve 1 g in 100 ml of *carbon dioxide-free water* with the aid of heat; add a drop of *metyl red solution* and titrate with *0.1N sodium hydroxide*. Not more than 0.5 ml is required for neutralisation.

Heavy metals : Not more than 10 parts per million, determined by Method A on a 2.0 g dissolved in 10 ml of *water*, add 2 ml of *dilute acetic acid Sp.*, and made upto 25 ml with *water*, Appendix 3.2.4.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *microcrystalline cellulose* as the coating substance and a mixture of 65 volumes of *n-butyl alcohol*, 15 volumes of *glacial acetic acid* and 25 volumes of *water* as the mobile phase. Apply separately to the plate 2 µl of each of three solutions in *methyl alcohol* containing (1) 10.0 per cent w/v of the substance being examined, (2) 0.25 per cent w/v of *methyldopa R.S.* and (3) 0.040 per cent w/v of *methyldopa R.S.* After removal of the plate allow it to dry in air, heat at 105° for ten minutes, and examine under an ultra-violet lamp having a maximum output at about 254 nm. The spot in the chromatogram obtained with solution (2) is more intense than any corresponding spot in the chromatogram obtained with solution (1). Expose the plate to the vapour of *iodine* for ten minutes and re-examine. The spot in the chromatogram obtained with solution (2) is more intense than any corresponding spot in the chromatogram obtained with solution (1) and the

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

spot in the chromatogram obtained with solution (3) is more intense than any spot in the chromatogram obtained with solution (1), other than the principal spot and the spot due to methyldopa.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Water : Between 10.0 and 13.0 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately about 0.2 g and dissolve in 15 ml of *anhydrous formic acid*, 30 ml of *glacial acetic acid* and 30 ml of *dioxan*. Add 0.1 ml of *crysta-violet solution* and titrate with *0.1N perchloric acid*. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02112 g of $C_{10}H_{13}NO_4$.

Storage : Store in well-closed and light-resistant containers.

Methyldopa Tablets

Category : Antihypertensive.

Dose : The equivalent of 0.5 to 3 g of anhydrous methyldopa daily, in divided doses.

Usual strengths : 125 mg; 250 mg; 500 mg.

Standards : Methyldopa Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of anhydrous methyldopa, $C_{10}H_{13}NO_4$. The tablets may be coated.

Identification : (A) A quantity of the powdered tablets equivalent to 10 mg of anhydrous methyldopa complies with **Identification** test (A) described under Methyldopa.

(B) Shake a quantity of the powdered tablets equivalent to 5 g of anhydrous methyldopa with 30 ml of *N hydrochloric acid* for ten to fifteen seconds, and immediately filter. Adjust the pH of the filtrate to 4.9 with *dilute ammonia solution*, filter, wash the precipitate with 15 ml of *water*, and dry "in vacuo" for sixteen hours. Reserve a portion of the residue for the test for **Optical rotation.** The remainder of the residue complies with **Identification** test (B) described under Methyldopa.

(C) To 10 mg of the powdered tablets add 2 ml of *0.1N sulphuric acid* and 2 ml of *ferrous sulphate-citrate solution*. Add 0.5 ml of *dilute ammonia solution*; a dark purple colour is immediately produced.

Optical rotation : Determine the content of $C_{10}H_{13}NO_4$ in the residue reserved in **Identification** test (B) by the **Assay** procedure described under Methyldopa. Weigh accurately a quantity of the residue equivalent to 0.39 g of $C_{10}H_{13}NO_4$ and dissolve in sufficient *aluminium chloride solution* to produce 10.0 ml. *Optical rotation* of the resulting solution, between −0.98° and −1.09°, Appendix 5.12.

Other requirements : Comply with the requirements stated under Tablets.

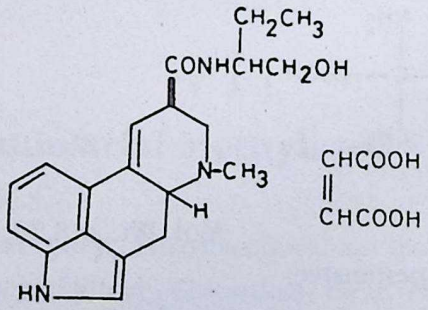
Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 0.1 g of anhydrous methyldopa, dissolve as completely as possible in sufficient *0.1N sulphuric acid* to produce 100.0 ml and filter. To 5.0 ml of the filtrate add 2 ml of *ferrous sulphate-citrate solution*, 8 ml of *glycine buffer solution*, and sufficient *water* to produce 100.0 ml. Measure the *extinction* of the resulting solution at the maximum at about 550 nm, Appendix 5.15 A. Calculate the content of $C_{10}H_{13}NO_4$, taking 89 as the value of E(1 per cent, 1-cm) at the maximum at about 550 nm.

Storage : Store in tightly-closed, light-resistant containers.

Labelling : The label on the container states the strength in terms of the equivalent amount of anhydrous methyldopa.

Methylergometrine Maleate

Methylergonovine Maleate



$C_{20}H_{25}N_3O_2, C_4H_4O_4$ Mol. Wt. 455.51

Category : Uterine stimulant; oxytocic.

Dose : By subcutaneous, intramuscular or intravenous injection, 0.1 to 0.2 mg.

Description : White or faintly yellow, crystalline powder; odourless; taste, bitter.

Solubility : Slightly soluble in *water*; soluble in *alcohol*.

Standards : Methylergometrine Maleate is the hydrogen maleate of methylergometrine, a partially synthetic homologue of ergometrine. It contains not less than 95.0 per cent and not more than the equivalent of 105.0 per cent of $C_{20}H_{25}N_3O_2, C_4H_4O_4$, calculated with reference to the dried substance.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Identification : (A) In the test for **Related substances** the principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained in solution (2).

(B) A solution has a blue fluorescence.

(C) Dissolve 0.25 mg in 1 ml of *glacial acetic acid* containing a trace of *ferric chloride*, carefully add 1 ml of *sulphuric acid* and shake well; a deep blue colour is produced.

Specific optical rotation : Between +44° and +50°, determined in a 0.5 per cent w/v solution, Appendix 5.12.

pH : Between 4.4 and 5.2, determined in a 0.02 per cent w/v solution, Appendix 5.10.

Related substances : Carry out the operations in subdued light and protect from light any solutions not immediately used. Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 10 volumes of *chloroform* and 1 volume of *methyl alcohol* as the mobile phase. Place a beaker containing 25 ml of *strong ammonia solution* in the developing chamber, cover the chamber, and allow to equilibrate for thirty minutes. Apply separately to the plate 25 µl of each of the following solutions in *methyl alcohol* containing (1) 0.4 per cent w/v of the substance being examined, (2) 0.4 per cent w/v of *methylergometrine maleate R.S.*, and (3) 0.012 per cent w/v of *methylergometrine maleate R.S.* After removal of the plate, allow it to dry in air and examine under in ultraviolet lamp having a maximum output at about 254 nm. Spray the plate with a solution containing 0.8 g of *dimethylaminobenzaldeyde* in a mixture of 80 g of *alcohol* and 20 g of *sulphuric acid*. Any spot in the chromatogram obtained with solution (1), other than the principal spot is not more intense than the spot in the chromatogram obtained with solution (3).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 2.0 per cent, determined on 0.5 g by drying "in vacuo at 100°", Appendix 5.8.

Assay : Weigh accurately about 20 mg and dissolve in sufficient *water* to produce 100.0 ml; dilute 20.0 ml to 100.0 ml with *water*. To 3.0 ml add 6 ml of *dimethylaminobenzaldehyde solution*, mix, cool in running water for five minutes, and add sufficient *dimethylaminobenzaldehyde solution* to produce 10.0 ml (solution A). At the same time prepare two similar solutions, one with *ergometrine maleate R.S.* (solution B) and the other without the substance being examined (solution C). Measure the *extinction* of a 1-cm layer of solution B at about 550 nm using solution C as the blank, Appendix 5.15 A. Without delay replace solution B with solution A, using the same cell, and measure the *extinction* of solution A at the same wavelength. Each mg of *ergometrine maleate R.S.* is equivalent to 1.032 mg of $C_{20}H_{25}N_3O_2, C_4H_4O_4$.

Storage : Store in an atmosphere of nitrogen, in sealed light-resistant tubes, in a cool place.

Methylergometrine Injection

Methylergonovine Injection

Category : Uterine stimulant

Dose : Methylergometrine Maleate. By subcutaneous, intramuscular, or intravenous injection, 0.1 to 0.2 mg.

Usual strength : 0.2 mg per ml.

Description : Clear, colourless solution with bluish fluorescence.

Standards : Methylergometrine Injection is a sterile solution of Methylergometrine Maleate in Water for Injection free from dissolved air. The acidity of the solution is adjusted to pH 3.2 by the addition of Maleic Acid. It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of $C_{20}H_{25}N_3O_2, C_4H_4O_4$.

Identification : (A) In the test for **Related substances** the principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

(B) Exhibits a blue fluorescence.

(C) To a volume equivalent to 0.1 mg of Methylergometrine Maleate, add 0.5 ml of *water* and 2 ml of *dimethylaminobenzaldehyde solution*; after about five minutes the mixture exhibits a deep blue colour.

pH : Between 2.7 and 3.5, Appendix 5.10.

Related substances : Complies with the test described under Methylergometrine Maleate. For solution (1) transfer a volume equivalent to 1 mg of Methylergometrine Maleate to a separator, add 1 ml of *sodium bicarbonate solution* and extract with three quantities, each of 5 ml, of *chloroform*. Evaporate the combined extracts to dryness at room temperature under reduced pressure. Dissolve the residue in 0.25 ml of *methyl alcohol*.

Other requirements : Complies with the requirements stated under Injections.

Assay : Protect the solutions from light throughout the Assay. Add sufficient *water* to produce a solution containing 0.04 mg of Methylergometrine Maleate per ml and complete the **Assay** described under Methylergometrine Maleate, beginning at the words "To 3.0 ml add.....".

Storage : Store in single-dose, light-resistant containers, in a cool place.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Methylergometrine Tablets

Methylergonovine Tablets

Category : Uterine stimulant.

Dose : Methylergometrine Maleate, 0.25 to 0.5 mg.

Usual strength : 0.125 mg.

Standards : Methylergometrine Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Methylergometrine Maleate, $C_{20}H_{25}N_3O_2, C_4H_4O_4$. The tablets may be coated.

Identification : (A) In the test for **Related substances** the principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

(B) Extract a quantity of the powdered tablets equivalent to 1 mg of Methylergometrine Maleate with 10 ml of *water*, filter, and wash the residue with sufficient *water* to produce 10 ml. The solution has a blue fluorescence. To 2 ml add 4 ml of *dimethylaminobenzaldehyde solution*; a deep blue colour is produced after few minutes.

Related substances : Comply with the test described under Methylergometrine Injection preparing solution (1) in the following manner: To a quantity of the powdered tablets equivalent to 1 mg of Methylergometrine Maleate add 5 ml of *water*, 1 ml of *sodium bicarbonate solution* and 2 ml of *chloroform*. Shake, allow to separate, and filter the chloroform layer through a plug of cotton wool moistened with *chloroform*. Repeat the extraction with a further 2 ml of *chloroform*, and filter. Evaporate the combined extracts to dryness at room temperature under reduced pressure and dissolve the residue in 0.25 ml of *methyl alcohol*; centrifuge, if necessary.

Uniformity of content : Crush one tablet and transfer to a separator with the aid of not more than 5 ml of *water*; add 3 ml of a 5.0 per cent w/v solution of *sodium bicarbonate*. Extract the mixture with four quantities, each of 5 ml, of *chloroform*. Filter the extracts through a plug of cotton-wool moistened with *chloroform* into a dry 100-ml separator. Add 2.0 ml of *water* and 10.0 ml of *dimethylaminobenzaldehyde solution* and shake vigorously for at least ninety seconds. Allow to stand for 30 minutes and then drain and discard the chloroform layer. Transfer the aqueous layer to a stoppered tube and allow to stand for sixty minutes. Measure the *extinction* of a 1-cm layer at the maximum at about 545 nm, using in the reference cell a mixture of 2.0 ml of *water* and 10.0 ml of *dimethylaminobenzaldehyde solution*, Appendix 5.15 A. Calculate the content of $C_{20}H_{25}N_3O_2, C_4H_4O_4$ per tablet, from the *extinction* obtained by carrying out the following operation simultaneously. Weigh accurately about 12 mg of *ergometrine maleate R.S.* in 200.0 ml of *water*. To 2.0 ml add 10 ml of *dimethylaminobenzaldehyde solution*, mix, cool in running water for five minutes; measure the *extinction* of a 1-cm cell at the maximum at about 545 nm, using in the reference cell a mixture of 2.0 ml of *water* and 10.0 ml of *dimethylaminobenzaldehyde solution*. Each mg of *ergometrine maleate R.S.* is equivalent to 1.032 mg of $C_{20}H_{25}N_3O_2, C_4H_4O_4$.

Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 90 and 110 per cent of the average except that for one tablet the content may be between 80 and 120 per cent of the average.

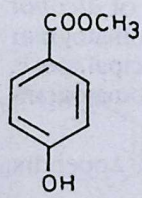
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Dissolve a quantity of the powder equivalent to 2 mg of Methylergometrine Maleate in 50 ml of a 1 per cent w/v solution of *tartaric acid* and complete the **Assay** described under Methylergometrine Maleate, beginning at the words "To 3.0 ml.....".

Storage : Store in tightly-closed, light-resistant containers.

Methylparaben

Methyl Hydroxybenzoate, Methyl Parahydroxybenzoate



$C_8H_8O_3$ Mol. Wt. 152.15

Category : Pharmaceutical aid (antifungal preservative).

Description : Small, colourless crystals or white, crystalline powder; odourless or has a faint characteristic odour; taste, slight, burning.

Solubility : Slightly soluble in *water*, in *benzene* and in *carbon tetrachloride*; freely soluble in *alcohol* and in *ether*.

Standards : Methylparaben is methyl-4-hydroxybenzoate. It contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of $C_8H_8O_3$, calculated with reference to the dried substance.

Identification : (A) Boil 10 mg with 10 ml of *water*, cool

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

and add 0.05 ml of ferric chloride solution; a reddish-violet colour is produced.

(B) Dissolve 0.1 g in 2 ml of *alcohol*, boil, and add 0.5 ml of *mercury nitrate solution*; a precipitate is formed and the supernatant liquid becomes red.

Melting range : between 125° and 128°, Appendix 5.11.

Acidity : Heat 0.75 g with 15 ml of *water* at 80° for one minute, cool and filter; the filtrate is neutral or acid to litmus. To 10 ml of the filtrate add 0.2 ml of *0.1N sodium hydroxide* and 2 drops of *methyl red solution*; the solution is yellow.

Chloride : Heat 2 g with 100 ml of *water*, cool, add *water* to restore the original volume, and filter. To 50 ml of the filtrate add 1 ml of *nitric acid* and 1 ml of *N silver nitrate*; the opalescence produced is not greater than the *standard opalescence* in the *limit test for chlorides* Appendix 3.2.2.

Sulphate : To 10 ml of the filtrate obtained in the test for **chloride** add few drops of *dilute hydrochloric acid* and a few drops of *barium chloride solution*. No turbidity is produced within 10 minutes.

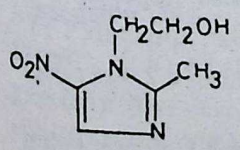
Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying over *silica gel* for five hours, Appendix 5.8.

Assay : Weigh accurately about 0.1 g, and boil for 30 minutes with 50 ml of *N sodium hydroxide*, replacing the water lost by evaporation. Cool, transfer to a glass-stoppered flask, and add immediately 50.0 ml of *0.1N bromine* and 10 ml of *hydrochloric acid*. Shake repeatedly during fifteen minutes, allow to stand for fifteen minutes, add 30 ml of *potassium iodide solution* and titrate the liberated iodine with *0.1N sodium thiosulphate*, using *starch solution* as indicator. Repeat the experiment with same quantities of the same reagents in the same manner, omitting the substance being examined. The difference between the titrations represents the amount of bromine required by methylparaben. Each ml of *0.1N bromine* is equivalent to 0.002536 g of $C_8H_8O_3$.

Storage : Store in well-closed containers.

Metronidazole



$C_6H_9N_3O_3$ Mol. Wt. 171.16

Category : Anti-amoebic; antitrichomonal; antigiardial.

Dose : For trichomoniasis, 200 mg three times daily, for 7 days.

For amoebiasis, 400 mg three times daily, for 5 to 10 days.

For giardiasis, 2 g daily for three successive days for adults, 1 g for children and 400 mg daily for infants.

Description : White or cream-coloured, crystalline powder; odour, slight; taste, bitter and slightly saline.

Solubility : Sparingly soluble in *water*; slightly soluble in *alcohol*, in *chloroform*, and in *solvent ether*.

Standards : Metronidazole is 2-(2-methyl-5-nitroimidazol-1-yl) ethanol. It contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of $C_6H_9N_3O_3$, calculated with reference to the dried substance.

Identification : (A) Dissolve 0.1 g in 4 ml of *N sulphuric acid*, add 10 ml of *picric acid solution*, and allow to stand for one hour; the precipitate after washing with cold *water* under suction and drying at 105° melts at about 150°, Appendix 5.11.

(B) Heat 10 mg in a water-bath for five minutes with 10 mg of *zinc powder*, 1 ml of *water* and 0.25 ml of *hydrochloric acid*, cool in ice, add 0.5 ml of *sodium nitrite solution*, and remove the excess of nitrite with *sulphamic acid*. Add 0.5 ml of the product to a mixture of 0.5 ml of *β-naphthol solution* and 2 ml of *sodium hydroxide solution*; an orange-red colour is produced.

(C) The light absorption in the range 230 to 350 nm of a 1-cm layer of a 0.001 per cent w/v solution in *0.1N hydrochloric acid* exhibits a maximum only at 277 nm; *extinction* at 277 nm, about 0.38, Appendix 5.15 A.

Melting range : Between 159° and 162°, Appendix 5.11.

2-Methyl-5-nitroimidazole : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel GF 254* as the coating substance and *acetone* as the mobile phase. Apply separately to the plate 10 µl of each of two solutions in a mixture of equal volumes of *methyl alcohol* and *chloroform* containing (1) 4.0 per cent w/v of the substance being examined and (2) 0.02 per cent w/v of *2-methyl-5-nitroimidazole R.S.* After removal of the plate, allow the solvent to evaporate, and examine under an ultra-violet lamp having a maximum output at about 254 nm; the spot in the chromatogram obtained with solution (2) is more intense than any corresponding spot in the chromatogram obtained with solution (1).

Heavy metals : Not more than 50 parts per million determined on 0.4 g by Method B, Appendix 3.2.4.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.45 g and dissolve in 10 ml of *glacial acetic acid*, add a few drops of *1-naphthol-benzein solution* and titrate with *0.1N perchloric acid* until a pale-green colour is produced. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.01712 g of $C_6H_9N_3O_3$.

Storage : Store in well-closed light-resistant containers.

Metronidazole Tablets

Category : Anti-amoebic; antitrichomonal; antigiardial.

Dose : Metronidazole. For trichomoniasis, 200 mg three times daily, for 7 days.

For amoebiasis, 400 mg three times daily, for 8 to 10 days.

For giardiasis, 2 g daily for three successive days for adults, 1 g daily for children and 400 mg daily for infants.

Usual strengths : 200 mg; 400 mg.

Standards : Metronidazole Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Metronidazole, $C_6H_9N_3O_3$. The tablets may be coated.

Identification : (A) Shake a quantity of the powdered tablets equivalent to about 0.2 g of Metronidazole with 4 ml of *N sulphuric acid* and filter. To the filtrate add 10 ml of *picric acid solution* and alow to stand for one hour, the precipitate after washing with cold *water* under suction and drying at 105° melts at about 150°, Appendix 5.11.

(B) Comply with **Identification** test (B) described under Metronidazole, using a quantity of the powdered tablets equivalent to 10 mg of Metronidazole.

2-Methyl-5-nitroimidazole : Comply with the test described under Metronidazole, using as solution (1), a solution prepared in the following manner: Shake a quantity of the powdered tablets equivalent to 0.2 g of Metronidazole with 5 ml of mixture of equal volumes of *chloroform* and *methyl alcohol* for five minutes and filter. The chromatogram obtained with solution (1) may also show spots due to excipients.

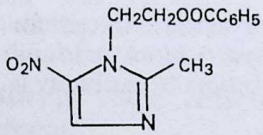
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 0.2 g of Metronidazole, transfer to a sintered-glass crucible and extract with six quantities, each of 10 ml, of hot *acetone*. Cool, add to the combined extracts 50 ml of *acetic anhydride*, 0.1 ml of a 1 per cent w/v solution of *brilliant green* in *glacial acetic acid* and titrate with *0.1N perchloric acid* to a yellowish-green end-point. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.01712 g of $C_6H_9N_3O_3$.

Storage : Store in well-closed, light-resistant containers.

Metronidazole Benzoate

Benzoyl Metronidazole



$C_{13}H_{13}N_3O_4$ Mol. Wt. 275.27

Category : Anti-amoebic.

Dose : For amoebic dysentry, the equivalent of 400 mg of metronidazole three times, daily, for 5 to 10 days.

NOTE – 200 mg of Metronidazole Benzoate is approximately equivalent to 125 mg of metronidazole.

Description : White or cream-coloured crystalline powder, odourless; almost tasteless.

Solubility : Sparingly soluble in *water*; soluble in *chloroform*, in *acetone*, and in *alcohol (90 per cent)*.

Standards : Metronidazole Benzoate is 2-(2-methyl-5-nitro-imidazol-1-yl) ethyl benzoate. It contains not less than 98.0 per cent of $C_{13}H_{13}N_3O_4$, calculated with reference to the dried substance.

Identification : (A) The light absorption, in the range 230 to 530 nm of a 1-cm layer of a 0.001 per cent w/v solution in *ethyl alcohol* exhibits a maximum only at 309 nm; *extinction* at 309 nm, about 0.3, Appendix 5.15 A.

(B) It gives the reactions of *benzoates*, Appendix 3.1.

Melting range : Between 100° and 102°, Appendix 5.11.

pH : Between 5.0 and 7.0, determined in a 2.0 per cent w/v suspension, Appendix 5.10.

Free benzoic acid : Not more than 0.2 per cent, determined by the following method: Dissolve 0.50 g in 25 ml of *alcohol* and titrate with *0.1N sodium hydroxide*, using *phenol red solution* as indicator. Perform a blank determination and make any necessary correction. Each ml of

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

0.1N sodium hydroxide is equivalent to 0.01221 g of $C_7H_6O_2$.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel HF 254* as the coating substance and a mixture of 8 volumes of *chloroform* and 2 volumes of *acetone* as the mobile phase. Apply separately to the plate 10 µl of each of three solutions in a mixture of equal volumes of *methyl alcohol* and *chloroform* containing (1) 6.0 per cent w/v of the substance being examined; (2) 0.02 per cent w/v of *2-methyl-5-nitroimidazole R.S.* and; (3) 0.02 per cent w/v of *metronidazole R.S.* After removal of the plate, allow the solvent to evaporate and examine under an ultra-violet lamp having a maximum output at about 254 nm. The spots in the chromatogram obtained with solutions (2) and (3) are more intense than any corresponding spots in the chromatogram obtained with solution (1).

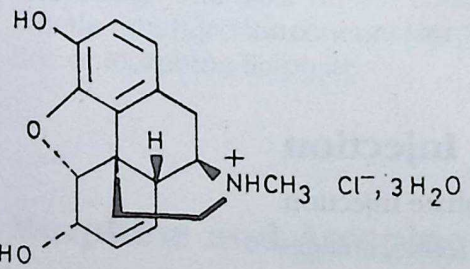
Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying "in vacuo at 60°," Appendix 5.8.

Assay : Weigh accurately about 0.5 g and dissolve in 50 ml of *acetone*. Add 10 ml of *acetic anhydride* and titrate with *0.1N perchloric acid* using *brilliant green solution* as indicator. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02753 g of $C_{13}H_{13}N_3O_4$.

Storage : Store in well-closed, light-resistant containers.

Morphine Hydrochloride



$C_{17}H_{19}NO_3, HCl, 3H_2O$ Mol. Wt. 375.85

Category : Narcotic, analgesic.

Dose : 10 to 20 mg.

Description : Colourless, glistening needles or white crystalline powder; odourless; taste, bitter.

Solubility : Soluble in *water*; sparingly soluble in *alcohol*; practically insoluble in *solvent ether* and in *chloroform*; soluble in *glycerin*.

Standards : Morphine Hydrochloride is the trihydrate of the hydrochloride of 7,8-didehydro-4,5α-epoxy-17-methylmorphinan-3,6α-diol, which may be obtained from opium. It contains not less than 98.0 per cent and not more than the equivalent of 100.5 per cent of $C_{17}H_{19}NO_3$, HCl, calculated with reference to the dried substance.

Identification : (A) Sprinkle a small quantity in powder form on the surface of a drop of *nitric acid*; an orange-red colour is produced.

(B) To a 2 per cent w/v solution add *potassium ferricyanide solution* containing 1 drop per ml of *ferric chloride test-solution*; an immediate bluish-green colour is produced (distinction from codeine).

(C) Add 5 ml of *sulphuric acid* to 5 mg in a test-tube, and add 1 drop of *ferric chloride test solution*, and heat in boiling water for two minutes; a deep blue colour is produced. Add a drop of *nitric acid*; the colour changes to dark red-brown (codeine and ethylmorphine give the same colour reactions, but dihydromorphine and papaverine do not produce this colour change).

(D) Add to about 1 mg of the powdered substance in a porcelain dish 0.5 ml of *sulphuric acid* containing 1 drop of *formaldehyde solution*. A purple colour is formed which turns to violet.

(E) Dissolve about 5 mg in 5 ml of *water*, and add 1 ml of *hydrogen peroxide solution*, 1 ml of *dilute ammonia solution* and 1 drop of a 4 per cent w/v solution of *copper sulphate*. A transient red colour develops.

(F) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

Acidity or Alkalinity : Dissolve 0.2 g in 10 ml of freshly boiled and cooled *water* add 1 drop of *methyl red solution*. Not more than either 0.2 ml of *0.02N sodium hydroxide* or of *0.02N hydrochloric acid* is required to change the colour of the solution.

Specific optical rotation : Between −112° and −115°, calculated with reference to the dried substance and determined in a 2 per cent w/v solution, Appendix 5.12.

Ammonium salts : Heat 0.2 g with *sodium hydroxide solution* on a water-bath for one minute; no odour of ammonia is perceptible.

Other alkaloids : Not more than 1.5 per cent, calculated with reference to the dried substance, determined by the following method: Transfer 0.5 g to a separator, add 15 ml of *water*, 5 ml of *N sodium hydroxide*, and 10 ml of *chloroform*, shake, allow to separate, and transfer the chloroform solution to another separator. Repeat the extraction with two further quantities, each of 10 ml, of *chloroform*. Wash the mixed chloroform solutions with 10 ml of *0.1N sodium hydroxide* and then with two successive quantities, each of 5 ml, of *water*, evaporate to dryness on a water-bath, and dry the residue to constant weight at 105°.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Meconate : Dissolve 0.2 g in 10 ml of freshly boiled and cooled *water*, add 1 ml of *hydrochloric acid* and a few drops of *ferric chloride test-solution*. No red colour develops.

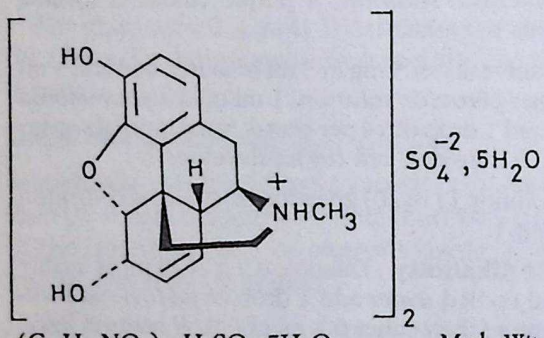
Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Between 11.5 per cent and 14.5 per cent, determined on 1.0 g by drying in an oven at 130°, Appendix 5.8.

Assay : Weigh accurately about 0.4 g of the dried substance in 30 ml of *glacial acetic acid*, add 10 ml of *mercuric acetate solution* and titrate with *0.1N perchloric acid*, using *crystal-violet solution* as indicator until the colour changes from blue to green-blue. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.03218 g of $C_{17}H_{19}NO_3,HCl$.

Storage : Store in well-closed, light-resistant containers.

Morphine Sulphate



$(C_{17}H_{19}NO_3)_2,H_2SO_4,5H_2O$ Mol. Wt. 758.83

Category : Narcotic, analgesic.

Dose : 10 to 20 mg.

By subcutaneous or intramuscular injection, 10 to 20 mg.

Description : White acicular crystals or cubical masses or white crystalline powder; odourless; taste, bitter.

Solubility : Soluble in *water*; freely soluble in hot *water*; slightly soluble in *alcohol* but more soluble in hot *alcohol*; insoluble in *chloroform* and in *solvent ether*.

Standards : Morphine Sulphate is the pentahydrate of the sulphate of 7,8-didehydro-4,5α-epoxy-17-methylmorphinan-3,6α-diol, which may be obtained from opium. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $(C_{17}H_{19}NO_3)_2,H_2SO_4$, calculated with reference to the dried substance.

Identification : (A) Complies with **Identification** tests (A) to (D) described under Morphine Hydrochloride.

(B) A solution (1 in 20) gives the reactions of *sulphates*, Appendix 3.1.

Specific optical rotation : Between −107° and −109.5°, calculated with reference to the dried substance and determined in a 2.0 per cent w/v solution, Appendix 5.12.

Acidity : Dissolve 0.2 g in 10 ml of freshly boiled and cooled *water* and titrate with *0.02N sodium hydroxide* using *methyl red solution* as indicator; not more than 0.2 ml of *0.02N sodium hydroxide* is required.

Ammonium salts : Heat 0.2 g with 5 ml of *sodium hydroxide solution* on a water-bath for one minute; no odour of ammonia is perceptible.

Other alkaloids : Complies with the test described under Morphine Hydrochloride.

Chloride : To 10 ml of a 1 per cent w/v solution, add 1 ml of *dilute nitric acid* and 1 ml of *silver nitrate solution*; no precipitate or turbidity is produced immediately.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Between 9.0 per cent and 12.0 per cent, determined on 1.0 g by drying in an oven at 145° for one hour, Appendix 5.8.

Assay : Carry out the **Assay** described under Morphine Hydrochloride, using 0.5 g, accurately weighed. Each ml of *0.1N perchloric acid* is equivalent to 0.06688 g of $(C_{17}H_{19}NO_3)_2,H_2SO_4$.

Storage : Store in well-closed, light-resistant containers.

Morphine Injection

Morphine Sulphate Injection

Category : Narcotic, analgesic.

Dose : Morphine Hydrochloride or Morphine Sulphate, by subcutaneous or intramuscular injection, 10 to 20 mg.

Usual strength : 10 mg per ml.

Standards : Morphine Injection is a sterile solution of Morphine Hydrochloride, or Morphine Sulphate, in Water for Injection. Suitable preservatives totalling not more than 0.5 per cent may be added. It contains not less than 93.0 per cent and not more

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

than 107.0 per cent of the stated amount of $C_{17}H_{19}NO_3, HCl, 3H_2O$ or $(C_{17}H_{19}NO_3)_2, H_2SO_4, 5H_2O$.

Identification : (A) To a suitable volume add *dilute ammonia solution* until alkaline; extract with 25 ml of a mixture of 1 volume of *alcohol* and 3 volumes of *chloroform* and evaporate the solution to dryness; the residue complies with **Identification** tests (A) and (B) described under Morphine Hydrochloride.

(B) It gives the reactions of *chlorides* or of *sulphates*, Appendix 3.1.

pH : Between 2.5 and 6.0. Appendix 5.10.

Other requirements : Complies with the requirements stated under Injection.

Assay : To an accurately measured volume equivalent to about 75 mg of morphine, add sufficient *sodium chloride* to saturate the solution, add *dilute ammonia solution*, dropwise, until just distinctly alkaline to *litmus*, and extract the alkaloid completely by shaking with successive quantities each of 20 ml, of a mixture of a 1 volume of *alcohol* and 3 volumes of *chloroform*. Wash the combined extracts with 5 ml of *water*, and extract the water twice with successive quantities, each of 3 ml of the alcohol-chloroform mixture. Filter the combined alcohol-chloroform extracts, and wash the separator and the filter with two quantities, each of 5 ml of the mixture. Evaporate the solution on a water-bath with the aid of a current of air to about 2 ml, add 25.0 ml of *0.02N sulphuric acid*, and heat gently to dissolve the morphine and to expel the remaining chloroform. Cool, add *methyl red solution* and titrate the excess acid with *0.02N sodium hydroxide*. Each ml of *0.02N sulphuric acid* is equivalent to 0.007516 g of $C_{17}H_{19}NO_3, HCl, 3H_2O$ or 0.007587 g of $(C_{17}H_{19}NO_3)_2, H_2SO_4, 5H_2O$.

Storage : Store in single-dose or multiple-dose, light-resistant containers.

Labelling : The label on the container also states whether the Injection contains Morphine Hydrochloride or Morphine Sulphate.

Morphine and Atropine Injection

Category : Narcotic, analgesic and anticholinergic.

Dose : By subcutaneous or intramuscular injection, 0.5 to 1.0 ml.

Standards : Morphine and Atropine Injection is a sterile solution of Morphine Sulphate and Atropine Sulphate in Water for Injection. It contains not less than 0.054 per cent w/v and not more than 0.066 per cent w/v of Atropine Sulphate $(C_{17}H_{23}NO_3)_2, H_2SO_4, H_2O$ and not less than 0.90 per cent w/v and not more than 1.1 per cent w/v of Morphine Sulphate $(C_{17}H_{19}NO_3)_2, H_2SO_4, 5H_2O$.

Identification : (A) Make the titrated liquid in the **Assay** for atropine sulphate alkaline by the addition of *sodium hydroxide solution* and extract with *chloroform*, evaporate the chloroform extracts; the residue complies with **Identification** tests (A) and (B) described under Atropine Sulphate.

(B) Saturate the titrated liquid in the **Assay** for morphine sulphate with *ammonium sulphate*; add *dilute ammonia solution* till distinctly alkaline and extract with a mixture of 3 volumes of *chloroform* and 1 volume of *alcohol*; evaporate the chloroform extract; the residue complies with the **Identification** tests (A) and (B) described under Morphine Sulphate.

Other requirements : Complies with the requirements stated under Injections.

Assay : *For atropine sulphate*—Measure 10 ml, add 10 ml of *water*, and 5 ml of *N sodium hydroxide*; extract with 15, 10 and 10 ml quantities of *chloroform* and continue the extraction with 10 ml quantities of *chloroform* till the alkaloid is completely extracted. Wash the chloroform extracts with the same 5 ml of *water* (reserve the aqueous solution and the washings). Evaporate off the chloroform, dissolve the residue in 2 ml of *alcohol*, add 2.0 ml of *0.05N sulphuric acid*, cool and titrate the excess of acid with *0.05N sodium hydroxide* using *methyl red solution* as indicator. Each ml of *0.05N sulphuric acid* is equivalent to 0.01737 g of $(C_{17}H_{23}NO_3)_2, H_2SO_4, H_2O$.

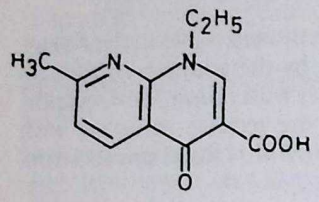
For morphine sulphate—Combine the aqueous solution and washings obtained in the **Assay** for atropine sulphate, add 1 g of *ammonium sulphate* and 25 ml of *alcohol* and extract with 40 ml followed by successive quantities of 40, 20 and 20 ml of a mixture of 1 volume of *alcohol* and 3 volumes of *chloroform*, washing each extract with the same two successive quantities of 5 ml of *water*, and carry out the extraction till the alkaloid is completely extracted; evaporate off the solvent, boil the residue with 10.0 ml of *0.1N sulphuric acid*, cool and titrate the excess of acid with *0.1N sodium hydroxide*, using *methyl red solution* as indicator. Each ml of *0.1N sulphuric acid* is equivalent to 0.03794 g of $(C_{17}H_{19}NO_3)_2, H_2SO_4, 5H_2O$.

Storage : Store in single-dose or multiple-dose, light-resistant containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Nalidixic Acid



$C_{12}H_{12}N_2O_3$ Mol. Wt. 232.24

Category : Antibacterial.

Dose : 2 to 4 g daily, in four divided doses.

Description : White to slightly yellow, crystalline powder; odourless.

Solubility : Practically insoluble in *water*; slightly soluble in *chloroform* and in *alcohol*; very slightly soluble in *solvent ether*; soluble in solutions of fixed alkali hydroxides and carbonates.

Standards : Nalidixic Acid is 1-ethyl-1,4-dihydro-7-methyl-4-oxo-1, 8-naphthyridine-3-carboxylic acid. It contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of $C_{12}H_{12}N_2O_3$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* of a potassium bromide dispersion exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *nalidixic acid R.S.*, Appendix 5.15 B.

(B) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of 0.0005 per cent w/v solution in *0.01N sodium hydroxide* exhibits maxima at 258 nm and 338 nm; *extinction* at 258 nm, about 0.56, Appendix 5.15 A.

Melting range : Between 225° and 231°, Appendix 5.11.

Heavy metals : Not more than 20 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

Sulphated ash : Not more than 0.2 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105° for two hours, Appendix 5.8.

Assay : Weigh accurately about 0.25 g and dissolve in 30 ml of *dimethyl formamide* which has been previously neutralised to *thymolphthalein solution* and titrate with *0.1N lithium methoxide*, using a magnetic stirrer and taking precautions against absorption of atmospheric carbon dioxide. Perform a blank determination and make any necessary correction. Each ml of *0.1N lithium methoxide* is equivalent to 0.02322 g of $C_{12}H_{12}N_2O_3$.

Storage : Store in tightly-closed, light-resistant containers.

Nalidixic Acid Tablets

Category : Antibacterial.

Dose : Nalidixic Acid, 1 g four times daily.

Usual strengths : 0.25 g and 0.5 g.

Standards : Nalidixic Acid Tablets contain not less than 93.0 per cent and not more than 107.0 per cent of the stated amount of Nalidixic Acid, $C_{12}H_{12}N_2O_3$.

Identification : (A) The light absorption, in the range 230 to 350 nm, of the solution obtained in the **Assay**, exhibits maxima at 258 nm and 334 nm, Appendix 5.15 A.

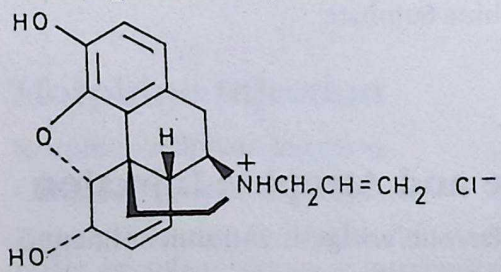
(B) Dissolve a quantity of the powdered tablets, equivalent to about 100 mg of Nalidixic Acid, in 50 ml of *chloroform*, shake for 15 minutes, and filter. Evaporate the filtrate to dryness on a water-bath; the residue after drying at 105° melts between 225° and 231°, Appendix 5.11.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.1 g of Nalidixic Acid and shake with 150 ml of *N sodium hydroxide* for three minutes. Dilute to 200.0 ml with *N sodium hydroxide*, mix well, and allow to stand for 15 minutes. Dilute 2.0 ml of this solution to 200.0 ml with *water* and measure the *extinction* of a 1-cm layer at the maximum at about 258 nm, Appendix 5.15 A, using *0.01N sodium hydroxide* as the blank. Calculate the content of $C_{12}H_{12}N_2O_3$, taking 1120 as the value of E(1 per cent, 1-cm) at the maximum at about 258 nm.

Storage : Store in well-closed, light-resistant containers.

Nalorphine Hydrochloride



$C_{19}H_{21}NO_3, HCl$ Mol. Wt. 347.84

Category : Antidote for narcotic analgesics.

Dose : By intravenous injection, 5 mg, repeated twice at 3 minute intervals if necessary.

Description : White or almost white, crystalline powder, slowly darkening on exposure to air and light; odourless.

208/DGHSNND/90—5,000 F-22

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

208/DGHS/ND/90—5,000 F-22

Solubility : Freely soluble in *water* and in dilute solutions of alkali hydroxides; sparingly soluble in *alcohol*; insoluble in *chloroform* and in *solvent ether*.

Standards : Nalorphine Hydrochloride is the hydrochloride of 17-allyl-7,8-didehydro-4,5α- epoxymorphinan-3,6α-diol. It contains not less than 97.0 per cent and not more than the equivalent of 103.0 per cent of $C_{19}H_{21}NO_3$,HCl, calculated with reference to the dried substance.

Identification : (A)To 10 ml of a 2.0 per cent w/v solution add 1 drop of *dilute ammonia solution*; a white precipitate soluble in *sodium hydroxide solution* is produced.

(B) Dissolve 2 mg in 2 ml of *water*, add 3 drops of *potassium ferricyanide solution* containing, in each ml, a drop of *ferric chloride test-solution*, a deep bluish-green colour is produced immediately.

(C) To 1 mg contained in a porcelain crucible add 0.5 ml of a 1 in 200 solution of *molybdic acid* in *sulphuric acid*; an intense purple colour is produced immediately.

(D) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.01 per cent w/v solution in *0.1N sodium hydroxide* exhibits a maximum only at 298 nm: *extinction* at 298 nm, about 0.6, Appendix 5.15 A.

(E) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

Melting range : Between 260° and 263°, Appendix 5.11.

Specific optical rotation : Between −122° and −125°, calculated with reference to the dried substance, and determined in a 2.0 per cent w/v solution, Appendix 5.12.

Acidity : Dissolve 0.2 g in 10 ml of freshly boiled and cooled *water* and titrate with *0.02N sodium hydroxide*, using *methyl red solution* as indicator; not more than 0.2 ml of *0.02N sodium hydroxide* is required.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying "in vacuo at 100°" for two hours, Appendix 5.8.

Assay : Weigh accurately about 25 mg and dissolve in sufficient *water* to produce 250.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 285 nm, Appendix 5.15 A. Calculate the content of $C_{19}H_{21}NO_3$, HCl from the *extinction* obtained by repeating the **Assay** on 25 mg accurately weighed of *nalorphine hydrochloride R.S.* instead of the substance being examined.

Storage : Store in tightly-closed, light-resistant containers.

Nalorphine Injection

Nalorphine Hydrochloride Injection

Category : Antidote for narcotic analgesics.

Dose : Nalorphine Hydrochloride, by intravenous injection, initial dose, 5 to 10 mg, to be repeated in accordance with the needs of the patient so that the total dose does not exceed 40 mg.

Usual strength : 10 mg in 1 ml.

Standards : Nalorphine Injection is a sterile solution of Nalorphine Hydrochloride in Water for Injection. It is suitably buffered. It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of $C_{19}H_{21}NO_3$, HCl.

Identification : (A) To a volume equivalent to 0.2 g of Nalorphine Hydrochloride add 1 drop of *dilute ammonia solution*; a white precipitate soluble in *sodium hydroxide solution* in produced.

(B) It gives the reactions of *chlorides*, Appendix 3.1.

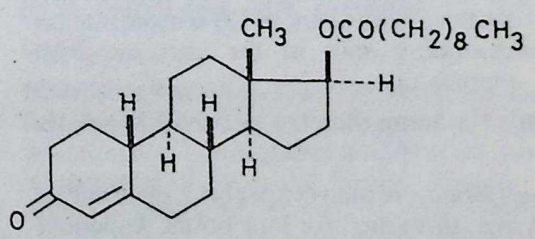
pH : Between 6.0 to 7.5, Appendix 5.10.

Other requirements : Complies with the requirements stated under Injections.

Assay : Transfer an accurately measured volume equivalent to about 10 mg of Nalorphine Hydrochloride, to a separator, add 1 ml of *dilute hydrochloric acid*, and dilute to about 10 ml with *water*. Extract with five successive quantities, each of 5 ml, of *chloroform*, allowing the layers to separate before drawing off each chloroform extract and discard the chloroform extracts. Transfer the aqueous layer to a 100-ml volumetric flask with the aid of *water*, dilute to volume with *water*, and mix. Continue as directed in the **Assay** under Nalorphine Hydrochloride, beginning at the words "Measure the *extinction*.....".

Storage : Store in light-resistant containers.

Nandrolone Decanoate



$C_{28}H_{44}O_3$ Mol. Wt. 428.65

Category : Anabolic steroid; weak androgen.

Dose : By intramuscular injection, 25 to 50 mg.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Description : White to creamy-white, crystalline powder; odour, faint and characteristic.

Solubility : Practically insoluble in *water*; freely soluble in *alcohol*, soluble in *chloroform*, in *solvent ether*; in fixed oils, and in esters.

Standards : Nandrolone Decanoate is 3-oxo-4-estren-17β-yl decanoate. It contains not less than 97.0 per cent, not more than the equivalent of 103.0 per cent of $C_{28}H_{44}O_3$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* of a 5 per cent w/v solution in *carbon tetrachloride IR* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *nandrolone decanoate R.S.*, Appendix 5.15 B.

(B) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.001 per cent w/v solution in *alcohol* exhibits a maximum only at 239 nm; *extinction* at 239 nm, about 0.41, Appendix 5.15 A.

(C) Dissolve 25 mg in 1 ml of *methyl alcohol*, add 2 ml of *semicarbazide acetate solution*, heat under a reflux condenser for thirty minutes, and cool; the precipitate, after recrystallisation from *alcohol*, melts at about 175°, Appendix 5.11.

Melting range : Between 33° and 37°, Appendix 5.11.

Specific optical rotation : Between +32° and +36°, determined in a 2 per cent w/v solution in *dioxan*, Appendix 5.12.

Nandrolone : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 7 volumes of *heptane* and 3 volumes of *acetone* as the mobile phase. Apply separately to the plate 1 µl of each of two solutions in *chloroform* containing (1) 1.5 per cent w/v of substance being examined and (2) 0.03 per cent w/v of the *nandrolone R.S.* After removal of the plate, allow it to dry in air, until the odour of the solvent is no longer detectable, spray with a 10 per cent v/v solution of *sulphuric acid* in *alcohol*, heat at 105° for thirty minutes and examine under an ultra-violet lamp having a maximum output at about 366 nm. The spot in the chromatogram obtained with solution (2) is more intense than any corresponding spot in the chromatogram obtained with solution (1).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying "in vacuo" for four hours, Appendix 5.8.

Assay : Weigh accurately about 10 mg and dissolve in sufficient *ethyl alcohol* to produce 100.0 ml, dilute 5.0 ml to 50.0 ml with *ethyl alcohol*, and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 239 nm, Appendix 5.15 A, calculate the content of $C_{28}H_{44}O_3$, taking 407 as the value of E(1 per cent, 1-cm) at the maximum at about 239 nm.

Storage : Store under nitrogen in tightly-closed, light-resistant containers at a temperature between 2° and 10°.

Nandrolone Decanoate Injection

Category : Anabolic steroid, weak androgen.

Dose : Nandrolone Decanoate, by intramuscular injection, 25 to 50 mg.

Usual strength : 25 mg per ml.

Description : Colourless or very pale yellow, clear liquid.

Standards : Nandrolone Decanoate Injection is a sterile solution of Nandrolone Decanoate in Ethyl Oleate or other suitable ester, in a suitable fixed oil, or in any mixture of these. It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of $C_{28}H_{44}O_3$.

Identification : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 7 volumes of *heptane* and 3 volumes of *acetone* as the mobile phase. Apply separately to the plate 1 µl of each of two solutions prepared as follows: For solution (1), dilute the injection with *carbon tetrachloride* to give a solution containing the equivalent of 0.5 per cent w/v of Nandrolone Decanoate. For solution (2) mix 1 volume of *nandrolone decanoate solution R.S.* with 9 volumes of *carbon tetrachloride*. After removal of the plate, allow it to dry in air until the odour of the solvent is no longer detectable, spray with a 10 per cent v/v solution of *sulphuric acid* in *alcohol*, heat at 105° for thirty minutes, and examine under an ultra-violet lamp having a maximum output at about 366 nm. The principal spot in the chromatogram obtained with solution (1) corresponds with the principal spot in the chromatogram obtained with solution (2). Subsidiary spots due to the vehicle may also be observed.

Other requirements : Complies with the requirements stated under Injections.

Assay : To a volume equivalent to 0.1 g of Nandrolone Decanoate add sufficient *chloroform* to produce 100.0 ml. Dilute 3.0 ml to 50.0 ml with *chloroform*; to 5.0 ml add 10 ml of *isoniazid solution* and sufficient *methyl alcohol* to produce 20.0 ml. Allow to stand for 45 minutes and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 380 nm, using as the blank, 5 ml of *chloroform* treated in a similar manner, Appendix

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

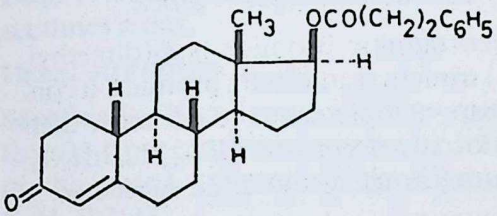
5.15 A. Calculate the content of $C_{28}H_{44}O_3$ from the *extinction* obtained by repeating the operation using a suitable quantity of *nandrolone R.S.* Each mg of *nandrolone R.S.* is equivalent to 1.570 mg of $C_{28}H_{44}O_3$.

Storage : Store in single-dose or multiple-dose, light-resistant containers.

Labelling : The label on the container states (1) the composition of the solvent; (2) "For intramuscular injection only".

Nandrolone Phenylpropionate

Nandrolone Phenpropionate



$C_{27}H_{34}O_3$ Mol. Wt. 406.56

Category : Anabolic steroid; weak androgen.

Dose : By intramuscular injection, 25 to 50 mg weekly.

Description : White to creamy-white, crystalline powder; odour, characteristic.

Solubility : Practically insoluble in *water*, soluble in *alcohol*, in *chloroform*, in *dioxan*, and in vegetable oils.

Standards : Nandrolone Phenylpropionate is 3-oxo-4-estren-17β-yl 3-phenylpropionate. It contains not less than 97.0 per cent and not more than the equivalent of 103.0 per cent of $C_{27}H_{34}O_3$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *nandrolone phenpropionate R.S.*, Appendix 5.15 B.

(B) The light absorption, in the range 230 to 350 nm, of a 0.001 per cent w/v solution in *alcohol* exhibits a maximum only at 240 nm; *extinction* at 240 nm, about 0.43, Appendix 5.15 A.

(C) Dissolve 25 mg in 1 ml of *methyl alcohol*, add 2 ml of *semicarbazide acetate solution*, heat under a reflux condenser for half an hour and cool; the precipitate melts at about 182°, Appendix 5.11.

(D) Complies with the test for *identification of steroids*, Appendix 3.3.11, using *solvent III* and *mobile phase F*.

Melting range : Between 95° and 99°, Appendix 5.11.

Specific optical rotation : Between +48° and +51°, determined in a 1.0 per cent w/v solution in *dioxan*, Appendix 5.12.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying "in vacuo" for four hours, Appendix 5.8.

Assay : Weigh accurately about 10 mg and dissolve in sufficient *ethyl alcohol* to produce 100.0 ml, dilute 5.0 ml to 50.0 ml with *ethyl alcohol* and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 240 nm, Appendix 5.15 A. Calculate the content of $C_{27}H_{34}O_3$, taking 430 as the value of E(1 per cent, 1-cm) at the maximum at about 240 nm.

Storage : Store in a tightly-closed, light-resistant containers.

Neomycin Sulphate

Category : Antibacterial (topical and systemic)

Dose : For systemic use, the equivalent of 0.7 g to 2.0 g of neomycin base daily, in divided doses.

Description : White or yellowish-white powder; odourless or almost odourless; hygroscopic.

Solubility : Freely soluble in *water*; very slightly soluble in *alcohol*; insoluble in *acetone*, in *chloroform* and in *solvent ether*.

Standards : Neomycin Sulphate is a mixture of the sulphates of substances produced by the growth of certain selected strains of *Streptomyces fradiae*. It contains an amount of neomycin sulphate equivalent to not less than 600 µg per mg of neomycin base, calculated with reference to the dried substance.

Identification : (A) Dissolve about 10 mg in 5 ml of *water*, add 0.1 ml of *pyridine* and 2 ml of a 0.1 per cent w/v solution of *ninhydrin* and heat on a water-bath at a temperature of about 70° for ten minutes. A deep violet colour is produced.

(B) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel H* as the coating substance and a freshly prepared 3.85 per cent w/v solution of *ammonium acetate* as the mobile phase. Apply separately to the plate 1 µl of each of two solutions

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

containing (1) 2 per cent w/v of the substance being examined and (2) 2 per cent w/v of *neomycin sulphate R.S.* After removal of the plate, allow it to dry in air for ten minutes, heat at 100° for one hour and spray with a 0.1 per cent w/v solution of *ninhydrin* in *n-butyl alcohol* saturated with *water*. Heat again at 100° for five minutes. The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

(C) A solution (1 in 20) gives the reactions of *sulphates*, Appendix 3.1.

pH : Between 5.0 and 7.5, determined in a 10 per cent w/v solution, Appendix 5.10.

Neamine : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel H* as the coating substance and a freshly prepared 3.85 per cent w/v solution of *ammonium acetate* as the mobile phase. Apply separately to the plate 1 µl of each of two solutions containing (1) 0.40 per cent w/v of the substance being examined, and (2) 0.0080 per cent w/v of *neamine hydrochloride R.S.* After removal of the plate, allow it to dry in a current of warm air, heat at 110° for ten minutes, spray the hot plate with *sodium hypochlorite solution* diluted with *water* immediately before use to contain about 0.5 per cent w/v of available chlorine, and dry in a current of cold air until a sprayed area of the plate below the line of application gives at most a very faint blue colour with 0.05 ml of *starch-iodide solution*; avoid prolonged exposure to the cold air. Spray the plate with *starch-iodide solution*. The spot in the chromatogram obtained with solution (2) is more intense than any corresponding spot in the chromatogram obtained with solution (1).

Sulphated ash : Not more than 1.0 per cent, Appendix 3.2.7.

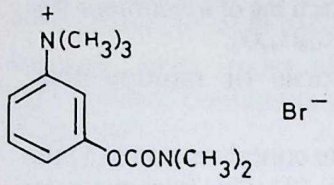
Loss on drying : Not more than 6.0 per cent, determined on 1.0 g by drying "in vacuo at 60°" for three hours, Appendix 5.8.

Assay : Carry out the *microbiological assay of antibiotics, Method A*, Appendix 4.1, and express the results in µg of neomycin base per mg.

Storage : Store in tightly-closed, light-resistant containers in a cool place.

Labelling : The label on the container states (1) the strength in terms of µg of neomycin per mg; (2) the date after which the contents are not intended to be used; (3) the storage conditions.

Neostigmine Bromide



$C_{12}H_{19}BrN_2O_2$ Mol. Wt. 303.20

Category : Cholinergic.

Dose : 15 to 30 mg, three to six times a day.

Description : White, crystalline powder; odourless; taste, bitter.

Solubility : Very soluble in *water*; soluble in *alcohol*; practically insoluble in *solvent ether*.

Standards : Neostigmine Bromide is 3-(dimethylcarbamoyloxy) trimethyl anilinium bromide. It contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of $C_{12}H_{19}BrN_2O_2$, calculated with reference to the dried substance.

Identification : (A) Warm about 50 mg with 1 ml of *dilute sodium hydroxide solution*; an odour of *dimethylamine* develops slowly.

(B) Warm about 50 mg with 0.4 g of *potassium hydroxide* and 2 ml of *alcohol* on a water-bath for three minutes, replacing the evaporated *alcohol*. Cool, add 2 ml of *water* and 2 ml of *diazobenzenesulphonic acid solution*. A red colour develops.

(C) The light absorption, in the range 230 to 350 nm, of a 0.02 per cent w/v solution in *0.5N sulphuric acid* exhibits maxima at 260 nm and at 266 nm, Appendix 5.15 A.

(D) A solution (1 in 50) gives the reactions of *bromides*, Appendix 3.1.

Melting range : Between 171° and 176°, with decomposition, Appendix 5.11.

Acidity : Dissolve 0.2 g in 20 ml of *carbon dioxide-free water* and titrate to pH 7.0 with *0.02N sodium hydroxide (carbonate-free)*; not more than 0.1 ml is required.

Sulphate : Dissolve 0.25 g in 10 ml of *water*, add 1 ml of *dilute hydrochloric acid*, and 1 ml of *barium chloride solution*; no turbidity is produced immediately.

3-hydroxyphenyl trimethylammonium bromide : A solution of 1.0 g in 10 ml of *chloroform* is clear.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.75 g, dissolve in a mixture of 70 ml of *glacial acetic acid* and 20 ml of

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

mercuric acetate solution, add four drops of *crystal-violet solution* and titrate with *0.1N perchloric acid* to a blue end-point. Perform a blank determination, and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.0303 g of $C_{12}H_{19}BrN_2O_2$.

Storage : Store in well-closed, light-resistant containers.

Neostigmine Tablets

Neostigmine Bromide Tablets

Category : Cholinergic.

Dose : Neostigmine Bromide, 15 to 30 mg, three tc six times a day.

Usual strength : 15 mg.

Standards : Neostigmine Tablets contain not less than 93.0 per cent and not more than 107.0 per cent of the stated amount of Neostigmine Bromide, $C_{12}H_{19}BrN_2O_2$.

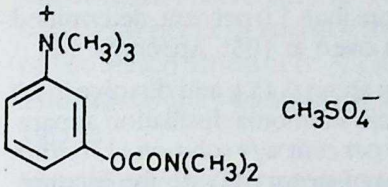
Identification : Triturate a quantity of the powdered tablets equivalent to about 0.3 g of Neostigmine Bromide with three quantities, each of 5 ml, of *solvent ether* and discard the ether. Macerate the residue with several quantities, each of 10 ml, of *alcohol* filtering after each maceration. Evaporate the combined filtrates on a water-bath, and dry the residue at 105° for one hour. The residue melts at 167°, with decomposition and complies with **Identification** tests (B) and (D) described under Neostigmine Bromide.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 0.15 g of Neostigmine Bromide, transfer to a semi-micro ammonia distillation apparatus, and add 20 ml of a 50 per cent w/v solution of *sodium hydroxide* and 0.5 ml of 2 per cent solution of *S-octyl alcohol* in *liquid paraffin*, and carry out the **Assay** described under Neostigmine Methylsulphate, beginning at the words "Pass a current of steam....". Each ml of *0.02N sulphuric acid* is equivalent to 0.006064 g of $C_{12}H_{19}BrN_2O_2$.

Storage : Store in well-closed, light-resistant containers.

Neostigmine Methylsulphate



$C_{13}H_{22}N_2O_6S$ Mol. Wt. 334.39.

Category : Cholinergic; antidote to curare principles.

Description : White crystalline powder, odourless; taste, bitter.

Solubility : Very soluble in *water*; soluble in *alcohol*.

Standards : Neostigmine Methylsulphate is 3-(dimethylcarbamoyloxy) trimethylanilinium methyl sulphate. It contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of $C_{13}H_{22}N_2O_6S$, calculated with reference to the dried substance.

Identification : (A) Place about 1 mg in a small porcelain dish, add 2 ml of *water* and 0.5 ml of *sodium hydroxide solution*, and evaporate on a steam-bath to dryness. Transfer the residue to a small test-tube, and quickly heat in a suitable liquid-bath to 250°, continuing at that temperature for about 30 seconds. Cool, dissolve the residue in 0.5 ml of *water*, cool in ice-water, and add 1 ml of *diazobenzenesulphonic acid solution*; a cherry-red colour is produced.

(B) Mix about 20 mg with 0.5 g of *sodium carbonate* and heat the mixture to fusion in a small crucible. Boil the fused mass with 10 ml of *water* until disintegrated, and filter. Add a few drops of *bromine* to the filtrate, heat to boiling, acidify with *hydrochloric acid*, and expel the excess bromine by boiling; the resulting solution gives the reactions of *sulphates*, Appendix 3.1.

(C) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.02 per cent w/v solution exhibits two maxima, at 260 nm and at 266 nm; *extinction* at 260 nm, and at 266 nm, about 0.24, Appendix 5.15 A.

Melting range : Between 142° and 149°, Appendix 5.11.

Acidity : Dissolve 0.2 g in 20 ml of *carbondioxide-free water* and titrate to pH 7.0 with *0.02N sodium hydroxide (carbonate-free)*; not more than 0.2 ml is required.

Sulphate : To 10 ml of a 2 per cent w/v solution, add 1 ml of *dilute hydrochloric acid* and 1 ml of *barium chloride solution*; no turbidity results immediately.

Chloride : To 10 ml of a 2.0 per cent w/v solution add 1 ml of *2N nitric acid* and 1 ml of *silver nitrate solution* no opalescence results immediately.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.15 g and dissolve in 20 ml of *water* in a semi-micro ammonia distillation apparatus, and add 20 ml of a 50 per cent w/v solution of *sodium hydroxide*. Pass a current of steam through the mixture collect the distillate in 50.0 ml of *0.1N sulphuric acid* until the total volume reaches about 200 ml, and titrate the excess of acid with *0.02N sodium hydroxide*, using *methyl red solution* as indicator. Repeat the experiment with the same quantities of the same reagents in the same manner, omitting Neostigmine Methylsulphate. Each ml of *0.02N sulphuric acid* is equivalent to 0.006688 g of $C_{13}H_{22}N_2O_6S$.

Storage : Store in well-closed, light-resistant containers.

Neostigmine Injection

Neostigmine Methylsulphate Injection

Category : Cholinergic; antidote to curare principles.

Dose : Neostigmine Methylsulphate. By intramuscular or subcutaneous injection, 0.25 to 2 mg in repeated doses as necessary.

By intravenous injection, 0.5 mg in 1 ml; 2.5 mg in 1 ml.

Usual strengths : 0.5 mg in 1 ml; 2.5 mg in 1 ml.

Standards : Neostigmine Injection is a sterile solution of Neostigmine Methylsulphate in Water for Injection. It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of $C_{13}H_{22}N_2O_6S$.

Identification : (A) Dilute, if necessary, a volume of the injection equivalent to 2.5 mg of Neostigmine Methylsulphate to 5 ml with *water*, shake with three quantities, each of 10 ml, of *solvent ether* and dilute the aqueous solution to 10 ml with *water*. The light absorption, in the range 230 to 350 nm of a 2-cm layer of the resulting solution exhibits maxima at 260 nm and at 266 nm, Appendix 5.15 A.

(B) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 50 volumes of *chloroform*, 35 volumes of *methyl alcohol*, 10 volumes of *formic acid* and 5 volumes of *water* as the mobile phase. Apply separately to the plate 10 µl of each of the following three solutions: (1) the injection being examined, diluted if necessary with *water* to produce a solution containing 0.05 per cent w/v of Neostigmine Methylsulphate; (2) a 0.05 per cent w/v solution of *neostigmine methylsulphate R.S.*; (3) a mixture of equal volumes of solutions (1) and (2). After removal of the plate, allow it to dry in air and spray with dilute *potassium iodobismuthate solution*. The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2). The principal spot in the third chromatogram appears as a single, compact spot.

(C) To 1 ml add 0.5 ml of *sodium hydroxide solution* and evaporate to dryness on a water-bath. Heat quickly in an oil-bath to about 250° and maintain at this temperature for about thirty seconds. Cool, dissolve the residue in 1 ml of *water*, cool in ice water, and add 1 ml of *diazotised sulphanilic acid solution*, a cherry-red colour is produced.

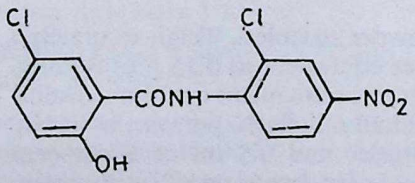
pH : Between 4.5 and 6.5, Appendix 5.10.

Other requirements : Complies with the requirements stated under Injections.

Assay : Measure accurately a volume equivalent to 30 mg of Neostigmine Methylsulphate and place in a semi-micro ammonia distillation apparatus, add 20 ml of a 50 per cent w/v solution of *sodium hydroxide* and carry out the **Assay** described under Neostigmine Methylsulphate, beginning at the words "Pass a current of steam .....". Each ml of *0.02N sulphuric acid* is equivalent to 0.006688 g of $C_{13}H_{22}N_2O_6S$.

Storage : Store in single-dose or multiple-dose, light-resistant containers.

Niclosamide



$C_{13}H_8Cl_2N_2O_4$ Mol. Wt. 327.13

Category : Anthelmintic (teniacide)

Dose : 2 g in divided doses.

Description : Cream-coloured powder, odourless; tasteless.

Solubility : Practically insoluble in *water*; slightly soluble in *alcohol*, in *chloroform* and in *solvent ether*.

Standards : Niclosamide is 2′, 5-dichloro-4′-nitrosalicylanilide. It contains not less than 98.0 per

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

cent of $C_{13}H_8Cl_2N_2O_4$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelength as, and have similar relative intensities to, those in the spectrum of *niclosamide R.S.*, Appendix 5.15 B.

(B) Burn 20 mg by the *oxygen-flask method*, Appendix 3.3.6, using 5 ml of *dilute sodium hydroxide solution* as the absorbing liquid. The resulting solution gives a white precipitate with *silver nitrate solution* which is insoluble in *dilute nitric acid* but soluble in *dilute ammonia solution*.

(C) Heat 50 mg with 5 ml of *N hydrochloric acid* and 0.1 g of *zinc powder* in a water-bath for 10 minutes, cool and filter. To the filtrate add 0.5 ml of a 1 per cent w/v solution of *sodium nitrite* and allow to stand for ten minutes; add 2 ml of a 2 per cent w/v solution of *ammonium sulphamate*, shake, allow to stand for ten minutes, and add 2 ml of a 0.5 per cent w/v solution of *N-(1-naphthyl) ethylenediamine hydrochloride*; a deep red colour is produced.

(D) It melts at about 228°, Appendix 5.11.

2-Chloro-4-nitroaniline : Boil 0.1 g with 20 ml of *methyl alcohol* for ten minutes, cool, add sufficient *N hydrochloric acid* to produce 50 ml and filter. To 10 ml of filtrate add 0.5 ml of 0.5 per cent w/v solution of *sodium nitrite* and allow to stand for ten minutes; add 1 ml of a 2 per cent w/v solution of *ammonium sulphamate*, shake, allow to stand for ten minutes and add 1 ml of a 0.5 per cent w/v solution of *N-(1-naphthyl) ethylenediamine hydrochloride*. The colour produced is not greater than that produced by simultaneously treating 10µg of 2-chloro-4-nitroaniline in the same manner.

5-Chlorosalicylic acid : Boil 0.50 g with 10 ml of *water* for two minutes, cool, filter, and add to the filtrate a few drops of *ferric chloride test-solution*; no red or violet colour is produced.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent determined on 1.0 g, by drying in an oven at 105°, Appendix 5.8.

Assay : Dissolve 0.3 g in 60 ml of *dimethylformamide* and titrate with *0.1N tetrabutylammonium hydroxide*, determining the end-point potentiometrically and taking care to avoid exposure to atmospheric carbon dioxide. Each ml of *0.1N tetrabutylammonium hydroxide* is equivalent to 0.03271 g of $C_{13}H_8Cl_2N_2O_4$.

Niclosamide Tablets

Category : Anthelmintic (teniacide)

Dose : Niclosamide, 2 g in divided doses.

Usual strength : 0.5 g.

Standards : Niclosamide Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Niclosamide, $C_{13}H_8Cl_2N_2O_4$. The tablets may contain sweetening and flavouring agents.

Identification : Heat a quantity of powdered tablets equivalent to 0.5 g of Niclosamide with 25 ml of *alcohol*, filter while hot, and evaporate to dryness on a water-bath. The residue complies with the **Identification** test described under Niclosamide.

2-Chloro-4-nitroaniline : Comply with the test described under Niclosamide, using a quantity of the powdered tablets equivalent to 0.10 g of Niclosamide.

5-Chlorosalicylic acid : Comply with the test described under Niclosamide, using a quantity of the powdered tablets equivalent to 0.50 g of Niclosamide.

Disintegration : The requirement for Disintegration does not apply to Niclosamide Tablets.

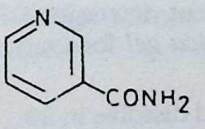
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Carry out the **Assay** described under Niclosamide, using a quantity of the powdered tablets equivalent to 0.12 g of Niclosamide.

Labelling : The label on the container states "Chew the tablets thoroughly before swallowing"

Nicotinamide

Niacinamide



$C_6H_6N_2O$ Mol. Wt. 122.13

Category : B-group Vitamin.

Dose : Prophylactic, 15 to 30 mg daily; therapeutic, 50 to 250 mg daily.

By intravenous injection, 50 to 250 mg daily.

Description : White, crystalline powder; almost odourless; taste, bitter.

Solubility : Freely soluble in *water* and in *alcohol*; soluble in *glycerin*; slightly soluble in *solvent ether*.

Standards : Nicotinamide is pyridine-3-carboxamide. It contains not less than 98.5 per cent and not more than the equivalent of 101.0 per cent of

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

$C_6H_6N_2O$, calculated with reference to the dried substance.

Identification : (A) Heat about 5.0 mg in a dry tube; pyridine is evolved.

(B) To 2 ml of a 0.1 per cent w/v solution add 6 ml of *cyanogen bromide solution* and 1 ml of 2.5 per cent v/v solution of *aniline*. A golden-yellow colour develops.

(C) Boil 0.1 g with 1 ml of *dilute sodium hydroxide solution*; ammonia is evolved (distinction from nicotinic acid).

Melting range : Between 128° and 131°, Appendix 5.11.

Clarity and colour of solution : Dissolve 7.5 g in 15 ml of *water*; the solution is clear and not more intensely coloured than a mixture of 0.5 ml of *ferric chloride C.S.*, 0.2 ml of *cobalt chloride C.S.*, 0.05 ml of *copper sulphate C.S.* and sufficient *water* to produce 15 ml.

pH : Between 5.5 and 8.0, determined in 5.0 per cent w/v solution, Appendix 5.10.

Chloride : 0.5 g complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphate : 0.5 g complies with the *limit test for sulphates*, Appendix 3.2.8.

Heavy metals : Not more than 30 parts per million, determined by Method A, Appendix 3.2.4, on a solution prepared by dissolving 0.67 g in 10 ml of *water*, 7.5 ml of *N hydrochloric acid* and sufficient *water* to produce 25 ml.

Nitro compounds : To 10 ml of a 5.0 per cent w/v solution add 1.0 ml of *10N sodium hydroxide* and allow to stand for five minutes; the solution is not more intensely coloured than a mixture of 0.4 ml of *ferric chloride C.S.*, 0.1 ml of *cobalt chloride C.S.* and sufficient *hydrochloric acid (1 per cent w/v)* to produce 10 ml.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying "in vacuo" over *silica gel* for four hours, Appendix 5.8.

Assay : Weigh accurately about 0.3 g and dissolve in 20 ml of *glacial acetic acid*, warming slightly if necessary to effect solution. Add 5 ml of *acetic anhydride* and 2 drops of *crystal-violet*, and titrate with *0.1N perchloric acid*. Perform a blank determination, and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.01221 g of $C_6H_6N_2O$.

Storage : Store in well-closed containers.

Nicotinamide Tablets

Niacinamide Tablets

Category : B-group Vitamin.

Dose : Nicotinamide. Prophylactic, 15 to 30 mg daily; therapeutic, 50 to 250 mg daily.

Usual strength : 50 mg.

Standards : Nicotinamide Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Nicotinamide, $C_6H_6N_2O$.

Identification : Extract a quantity of the powdered tablets equivalent to about 0.5 g of Nicotinamide, with two quantities, each of 10 ml of *alcohol*, evaporate the filtered extracts on a water-bath, and dry at 80° for two hours; the residue so obtained melts between 128° and 131° Appendix 5.11 and complies with **Identification** tests (A) and (B) described under Nicotinamide.

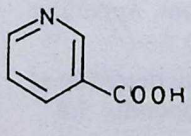
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 0.3 g of Nicotinamide, and boil gently with 200 ml of *water* and 75 ml of *sodium hydroxide solution* for twenty minutes in an ammonia distillation apparatus, collecting the distillate in 50.0 ml of *0.1N sulphuric acid*; boil vigorously to complete the distillation of ammonia, and titrate the excess acid with *0.1N sodium hydroxide*, using *methyl red solution* as indicator. Repeat the experiment with the same quantities of the reagents in the same manner, omitting the nicotinamide. The difference between the titrations represents the acid required to neutralise the ammonia evolved from nicotinamide. Each ml of *0.1N sulphuric acid* is equivalent to 0.01221 g of $C_6H_6N_2O$.

Storage : Store in well-closed containers.

Nicotinic Acid

Niacin



$C_6H_5NO_2$ Mol. Wt. 123.11

Category : B-group Vitamin; vasodilator.

Dose : Prophylactic, 15 to 30 mg, daily; therapeutic, 50 to 250 mg, daily.

Description : White or creamy-white crystals or crystalline powder; odourless; taste, feebly acid.

Solubility : Sparingly soluble in *water*, freely soluble in boiling *water*, and in boiling *alcohol*; practically insoluble in *solvent ether*; soluble in solutions of alkalis.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Standards : Nicotinic acid is 3-pyridinecarboxylic acid. It contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of $C_6H_5NO_2$, calculated with reference to the dried substance.

Identification : (A) Heat a small quantity with twice its weight of *soda lime*; pyridine is evolved.

(B) Dissolve about 50 mg in 20 ml of *water*, neutralise to *litmus paper* with *0.1N sodium hydroxide*, and add 3 ml of *copper sulphate solution*, a blue precipitate is gradually produced.

(C) To 2 ml of a 0.1 per cent w/v solution, add 6 ml of *cyanogen bromide solution* and 1 ml of a 2.5 per cent v/v solution of *aniline*, a golden-yellow colour is produced.

(D) Boil 20 mg with 5 ml of *sodium hydroxide solution*; no ammonia is evolved (distinction from nicotinamide).

Melting range : Between 234° and 237°, Appendix 5.11.

Heavy metals : Not more than 20 parts per million, determined by Method A, Appendix 3.2.4, on the following solution: Mix 1 g with 1.5 ml of *dilute hydrochloric acid*, add *water* to make 25 ml, heat gently until solution is complete and cool to room temperature.

Chlorides : 0.5 g complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphates : 0.5 g complies with the *limit test for sulphates*, Appendix 3.2.8.

Nitro compounds : Dissolve 0.1 g in 10 ml of *water*; the solution is clear. Add 1 ml of *2N sodium hydroxide*, the solution is not more intensely coloured than a mixture of 0.4 ml of *ferric chloride C.S.*, 0.1 ml of *cobalt chloride C.S.* and sufficient *hydrochloric acid (1 per cent w/v)* to produce 10 ml.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.3 g and dissolve in 50 ml of *carbon dioxide-free water* and titrate with *0.1N sodium hydroxide*, using *phenol red solution* as indicator. Each ml of *0.1N sodium hydroxide* is equivalent to 0.01231 g of $C_6H_5NO_2$.

Storage : Store in well-closed, light-resistant containers.

Nicotinic Acid Tablets

Niacin Tablets

Category : B-group vitamin.

Dose : Nicotinic acid. Prophylactic, 15 to 30 mg daily; therapeutic, 50 to 250 mg daily.

Usual strengths : 25 mg; 50 mg; 100 mg.

Standards : Nicotinic Acid Tablets contain not less than 93.0 per cent and not more than 107.0 per cent of the stated amount of Nicotinic Acid, $C_6H_5NO_2$.

Identification : (A) Triturate a quantity of the powdered tablets equivalent to 50 mg of Nicotinic Acid with 10 ml of *water* and filter. To 2 ml of the filtrate add 6 ml of *cyanogen bromide solution* and 1 ml of a 2.5 per cent v/v solution of *aniline*; a golden-yellow colour is produced.

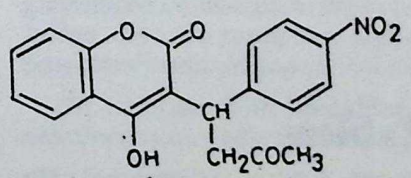
(B) Shake a quantity of the powdered tablets equivalent to 0.1 g of Nicotinic Acid with *alcohol*, filter and evaporate the filtrate to dryness. Add to the residue 10 mg of *citric acid* and 0.15 ml of *acetic anhydride* and heat on a water-bath; a reddish-violet colour is produced.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 0.3 g of Nicotinic Acid, add 40 ml of hot *alcohol*, previously neutralised to *phenolphthalein solution* and shake. Allow to stand for fifteen minutes, swirling occasionally, then shake for ten minutes. Filter through a cotton wool plug and wash the filter with *alcohol*. Add 50 ml of *carbon dioxide-free water* to the filtrate. Cool and titrate with *0.1N sodium hydroxide*, using *phenol red solution* as indicator. Each ml of *0.1N sodium hydroxide* is equivalent to 0.01231 g of $C_6H_5NO_2$.

Storage : Store in well-closed, light-resistant containers.

Nicoumalone



$C_{19}H_{15}NO_6$ Mol. Wt. 353.33.

Category : Anticoagulant.

Dose : Initial dose, 12 to 20 mg; subsequent doses, in accordance with the needs of the patient.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Description : White to brownish-white; almost odourless; taste, slightly sweet, becoming bitter.

Solubility : Practically insoluble in *water* and in *solvent ether*; slightly soluble in *alcohol* and in *chloroform*; soluble in solutions of alkali hydroxides.

Standards : Nicoumalone is 4-hydroxy-3-[1-(4-nitrophenyl)-3-oxobutyl] coumarin. It contains not less than 98.5 per cent of $C_{19}H_{15}NO_6$, calculated with reference to the dried substance.

Identification : (A) Heat 50 mg with 2.5 ml of *glacial acetic acid*, 0.5 ml of *hydrochloric acid*, and 0.2 g of *zinc powder* on a water-bath for five minutes, cool and filter; to the filtrate add 0.5 ml of *0.1N sodium nitrite* and add the mixture to 10 ml of a 1.0 per cent w/v solution of *β-naphthol* containing 3 ml of *sodium hydroxide solution*, a bright red precipitate is produced.

(B) The light absorption, in the range 230 to 350 nm of a 1-cm layer of a 0.001 per cent w/v solution in a mixture of 1 volume of *N hydrochloric acid* and 9 volumes of *methyl alcohol* exhibits maxima at 283 nm and 306 nm; *extinction* at 283 nm, about 0.65 and at 306 nm, about 0.5, Appendix 5.15 A.

(C) It melts at about 198°, Appendix 5.11.

Clarity and colour of solution : (1) A 1.0 per cent w/v solution in *ethyl acetate* is clear and almost colourless.

(2) A 2.0 per cent w/v solution in *sodium hydroxide solution* is clear and yellow.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.6 g, dissolve in 50 ml of *acetone* and titrate with *0.1N sodium hydroxide*, using *bromothymol blue solution* as indicator. Repeat the operation omitting the substance being examined; the difference between the titrations represents the amount of sodium hydroxide required. Each ml of *0.1N sodium hydroxide* is equivalent to 0.03533 g of $C_{19}H_{15}NO_6$.

Storage : Store in light-resistant containers.

Nicoumalone Tablets

Category : Anticoagulant.

Dose : Nicoumalone. Initial dose, 12 to 20 mg; subsequent doses, in accordance with the needs of the patient.

Usual strengths : 1 mg; 4 mg.

Standards : Nicoumalone Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Nicoumalone, $C_{19}H_{15}NO_6$.

Identification : (A) Heat a quantity of the powdered tablets equivalent to 50 mg of Nicoumalone with 30 ml of *acetone* under a reflux condenser for five minutes, filter, and wash the residue with two quantities, each of 10 ml, of *acetone*. Evaporate the combined filtrate and washings to 5 ml, add *water* dropwise until the solution becomes turbid, heat on a water-bath until the solution clears, and allow to stand. Filter, wash the crystals with a mixture of equal volumes of *acetone* and *water* and dry at 100° "in vacuo" for thirty minutes. The crystals comply with **Identification** test (A) described under Nicoumalone, using 25 mg for the test.

(B) The light absorption of the solution prepared as directed in the **Assay** exhibits maxima at 283 nm and 306 nm, Appendix 5.15 A.

Uniformity of content : Finely crush one tablet, add 30 ml of *methyl alcohol*, stir the mixture for thirty minutes, and filter through a sintered-glass crucible, washing the residue with three quantities, each of 15 ml, of *methyl alcohol*. To the combined filtrate and washings, add 10 ml of *N hydrochloric acid* and sufficient *methyl alcohol* to produce 100.0 ml. If necessary, dilute further with a solvent prepared by diluting 10 ml of *N hydrochloric acid* to 100 ml with *methyl alcohol* to give a solution containing about 1 mg of Nicoumalone in 100 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at about 306 nm, Appendix 5.15 A. Calculate the content of $C_{19}H_{15}NO_6$ taking 521 as the value of E(1 per cent, 1-cm) at the maximum at about 306 nm.

Repeat the operation using a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 85 and 115 per cent of the average except that for one tablet the content may be between 80 and 120 per cent of the average.

Other requirements : Comply with the requirements stated under Tablets.

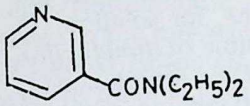
Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 1 mg of Nicoumalone, add 30 ml of *methyl alcohol*, stir the mixture for thirty minutes and filter through a sintered-glass crucible, washing the residue with three quantities, each of 15 ml, of *methyl alcohol*. To the combined filtrate and washings, add 10 ml of *N hydrochloric acid* and sufficient *methyl alcohol* to produce 100.0 ml and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 306 nm, Appendix 5.15 A. Calculate the content of $C_{19}H_{15}NO_6$, taking 521 as the value of E(1 per cent, 1-cm) at the maximum at about 306 nm.

Storage : Store in light-resistant containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Niketham ide



$C_{10}H_{14}N_2O$ Mol. Wt. 178.23

Category : Respiratory stimulant.

Dose : By subcutaneous, intramuscular or intravenous injection, 0.25 to 2 g.

Description : Colourless or yellowish oily liquid or crystalline mass; almost odourless or with a faint characteristic aromatic odour, taste, slightly bitter followed by a faint warm sensation on the tongue.

Solubility : Miscible with *water*, with *alcohol*, with *chloroform* and with *solvent ether*; slightly soluble in *benzene* and in *carbon tetrachloride*.

Standard : Nikethamide is *NN*-diethylpyridine-3-carboxamide. It contains not less than 98.0 per cent of $C_{10}H_{14}N_2O$.

Identification : (A) Heat 0.1 g with 1 ml of *dilute sodium hydroxide solution*; diethylamine is evolved progressively recognisable by its odour and by turning *red litmus paper* blue.

(B) Heat 0.1 g with 0.5 g of *sodium carbonate* until charring begins; pyridine, recognisable by its odour, is evolved.

(C) Mix 0.1 g with 0.5 ml of *copper sulphate solution*. An intense blue colour is formed. On addition of *potassium thiocyanate solution* a voluminous green precipitate is formed.

pH : Between 6.5 and 7.8, determined in a 25 per cent w/v solution, Appendix 5.10.

Congealing temperature : Between 23° and 24.5°, Appendix 5.5.

Wt. per ml : Between 1.058 to 1.066 g, Appendix 5.19.

Refractive index : Between 1.524 and 1.526, Appendix 5.14.

Clarity of solution : 0.2 g dissolves completely in 1 ml of *carbon disulphide* giving a clear solution.

Reducing substances : Mix 5 ml of a 25 per cent w/v solution with 3 drops of a 0.1 per cent w/v solution of *potassium permanganate*; the pink colour is not discharged within two minutes.

Other organic impurities : Dissolve 1 g in a mixture of 3 ml of *dilute hydrochloric acid* and 6 ml of *water*. Heat for one hour on a water-bath. Cool, and add 5 ml of a 20.0 per cent w/v solution of *sodium hydroxide*; the solution does not become distinctly yellow.

Free acid and free diethylamine : To a 10 per cent w/v solution, add five drops of *methyl red solution*; a yellow colour is produced. Add 0.1 ml of *0.1N hydrochloric acid*; the colour changes to red.

Nicotinic acid : To 5 ml of a 10 per cent w/v solution, add five drops of *dilute sulphuric acid*. Shake in a separator with two quantities, each of 20 ml, of a mixture of 3 volumes of *chloroform* and 1 volume of *isopropyl alcohol*. Filter the mixed extracts, evaporate to dryness on a water-bath, dissolve the residue in 10 ml of boiling *water*, cool and add 0.1 ml of *0.1N sodium hydroxide* and one drop of *phenolphthalein solution*; the solution turns red.

Heavy metals : Not more than 10 parts per million, determined by Method B on 2 g, Appendix 3.2.4.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Assay : Weigh accurately about 0.2 g and mix with 20 ml of *glacial acetic acid* and 5 ml of *acetic anhydride*. Titrate with *0.1N perchloric acid*, using *crystal-violet solution* as indicator. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.017820 g of $C_{10}H_{14}N_2O$.

Storage : Store in tightly-closed, light-resistant containers.

Nikethamide Injection

Category : Respiratory stimulant.

Dose : By subcutaneous, intramuscular, or intravenous injection, 1 to 4 ml (0.25 to 1 g of Nikethamide), repeated if necessary.

Description : Clear, colourless solution.

Standards : Nikethamide Injection is a sterile solution of Nikethamide in Water for Injection. It contains not less than 24.0 per cent w/v and not more than 26.0 per cent w/v of $C_{10}H_{14}N_2O$.

Identification : (A) Gives a voluminous precipitate with *alkaline potassium mercuri-iodide solution* and a greyish-brown flocculent precipitate with *tannic acid solution*. Gives no precipitate with *iodine solution* or with *potassium mercuri-iodide solution*.

(B) Complies with **Identification** tests (A) and (B); described under Nikethamide.

pH : Between 6.0 and 8.0, Appendix 5.10.

Other requirements : Complies with requirements stated under Injections.

Assay : Accurately measure a volume equivalent to about 0.3 g of Nikethamide and heat in a long-necked flask with 10 ml of a 50 per cent v/v solution of *nitrogen-free sul*

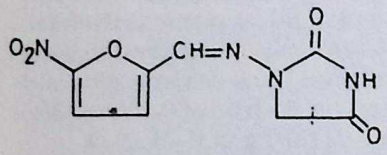
CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

phuric acid for two hours, cool, dilute with *water*, transfer to an ammonia distillation apparatus, add 50 ml of *sodium hydroxide solution* and distil the liberated diethylamine into 25.0 ml of *0.1N hydrochloric acid*. Titrate the excess of acid with *0.1N sodium hydroxide*, using *methyl red solution* as indicator. Repeat the operation without the preparation being examined; the difference between the titrations represents the acid required to neutralise the diethylamine formed. Each ml of *0.1N hydrochloric acid* is equivalent to 0.01782 g of $C_{10}H_{14}N_2O$.

Storage : Store in single-dose, light-resistant containers.

Nitrofurantoin



$C_8H_6N_4O_5$ Mol. Wt. 238.16 (anhydrous)

$C_8H_6N_4O_5,H_2O$ Mol. Wt. 256.17 (hydrous)

Category : Antibacterial (urinary).

Dose : 50 to 150 mg four times, daily.

Description : Lemon yellow crystals or fine powder; almost odourless; taste, bitter.

Solubility : Very slightly soluble in *water* and in *alcohol*; soluble in *dimethylformamide*.

Standards : Nitrofurantoin is 1-(5-nitrofurfurylidene-amino) imidazolidine-2, 4-dione. It is anhydrous or contains one molecule of water of hydration. It contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of $C_8H_6N_4O_5$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* of a dispersion in mineral oil exhibits maxima which are at the same wavelengths as and have similar relative intensities to, those in the spectrum of *nitrofurantoin R.S.*, Appendix 5.15 B.

(B) The light absorption, in the range 230 to 350 nm of a 1-cm layer of a 0.0005 per cent w/v solution in a mixture of 1 volume of *N hydrochloric acid* and 9 volumes of *methyl alcohol* exhibits two maxima at 266 nm and 367 nm; *extinction* at 367 nm, about 0.46, Appendix 5.15 A.

(C) Dissolve 5 mg in 5 ml of *0.1N sodium hydroxide*; a deep yellow solution is produced which becomes deep orange-red.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel HF 254* as the coating substance and a mixture of 10 volumes of *methyl alcohol* and 90 volumes of *nitromethane* as the mobile phase. Apply separately to the plate 10 µl of each of two solutions; for solution (1) dissolve 0.25 g in the minimum volume of *dimethylformamide* and dilute to 10 ml with *acetone*; for solution (2) dilute 1 volume of solution (1) to 100 volumes with *acetone*.

After removal of the plate, allow it to dry in air and heat at 105° for five minutes. Spray with a solution prepared by dissolving 0.75 g of *phenylhydrazine hydrochloride* in 50 ml of *water*, decolourising with *decolourising charcoal*, and adding 25 ml of *hydrochloric acid* and sufficient *water* to produce 200 ml. Heat the plate at 100° for a further ten minutes. Any spot in the chromatogram obtained with solution (1), other than the principal spot, is not more intense than any corresponding spot in the chromatogram obtained with solution (2).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Between 5.0 per cent and 7.1 per cent (hydrous form) and not more than 1.0 per cent (anhydrous form), determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Protect the solution from light throughout the assay.

Weigh accurately about 0.12 g and dissolve in 50 ml of *dimethylformamide*; add sufficient *water* to produce 1000.0 ml. Mix and dilute 5.0 ml to 100.0 ml with a solution containing 1.8 per cent w/v of *sodium acetate* and 0.14 per cent v/v of *glacial acetic acid*. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 367 nm, Appendix 5.15 A, using as the blank a 1 per cent v/v solution of *dimethylformamide* in the solution of sodium acetate and glacial acetic acid Calculate the content of $C_8H_6N_4O_5$, taking 765 as the value of E(1 per cent, 1-cm) at the maximum at about 367 nm.

Storage : Store in tightly-closed, light-resistant containers in a cool place.

Nitrofurantoin Tablets

Category : Antibacterial (urinary).

Dose : Nitrofurantoin, 50 to 150 mg four times, daily.

Usual strengths : 50 mg and 100 mg.

Standards : Nitrofurantoin Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Nitrofurantoin, $C_8H_6N_4O_5$.

Identification : The light absorption, in the range 220 to 400 nm, of the final solution obtained in the **Assay**, exhi-

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

bits two maxima, at 266 nm and 367 nm, Appendix 5.15 A.

Related substances : Comply with the test described under Nitrofurantoin, using as solution (1) a solution prepared in the following manner: Shake a quantity of the powdered tablets equivalent to 0.1 g of Nitrofurantoin with 10 ml of a mixture of 1 volume of *dimethylformamide* and 9 volumes of *acetone*, and filter.

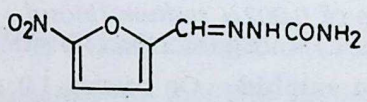
Other requirements : Comply with the requirements stated under Tablets.

Assay : Protect the solutions from light throughout the assay.

Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 0.12 g of Nitrofurantoin, add 50 ml of *dimethylformamide*, shake for five minutes, add sufficient *water* to produce 1000.0 ml, mix, and complete the **Assay** described under Nitrofurantoin beginning at the words "dilute 5.0 ml to 100.0 ml....." and filtering the final solution.

Storage : Store in well-closed, light-resistant containers, in a cool place.

Nitrofurazone



$C_6H_6N_4O_4$ Mol. Wt. 198.14

Category : Anti-infective, Antimicrobial (topical).

Description : Lemon yellow to brownish-yellow crystalline powder; odourless or almost odourless.

Solubility : Slightly soluble in *alcohol* and in *water*; practically insoluble in *chloroform* and in *solvent ether*.

Standards : Nitrofurazone is 5-nitro-2-furaldehyde semicarbazone. It contains not less than 97.0 per cent and not more than the equivalent of 103.0 per cent of $C_6H_6N_4O_4$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *nitrofurazone R.S.*, Appendix 5.15 B.

(B) The light absorption in the range 230 to 400 nm of a 0.001 per cent w/v solution prepared as directed in the **Assay** exhibits a maximum at about 375 nm and a minimum at about 306 nm, Appendix 5.15 A.

(C) Dissolve 0.4 g of *potassium hydroxide* in 10 ml of *alcohol*. Immediately before use dilute this solution to 100 ml with *dimethylformamide*. To 10 ml of this solution add a few crystals of Nitrofurazone; a purple colour is produced.

pH : Between 5.0 and 7.5, determined in a solution obtained by shaking 1 g with 100 ml of *water* for fifteen minutes and filtering, Appendix 5.10.

Related substances : Carry out in subdued light the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 95 volumes of *toluene* and 5 volumes of *dioxan* as the mobile phase. Apply separately to the plate 10 µl of each of two solutions in a mixture of equal volumes of *dimethylformamide* and *acetone* containing (1) 1 per cent w/v of the substance being examined and (2) 0.002 per cent w/v of *5-nitro-2-furfuraldazine R.S.* After removal of the plate, heat it at 105° for five minutes and spray with a solution prepared by dissolving 0.75 g of *phenylhydrazine hydrochloride* in 10 ml of *alcohol*, diluting to 50 ml with *water*, adding *decolourising charcoal*, filtering and then adding to the filtrate 25 ml of *hydrochloric acid* and sufficient *water*, to produce 200 ml. The spot in the chromatogram obtained with solution (2) is more intense than any corresponding spot in the chromatogram obtained with solution (1).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined by drying 1.0 g in an oven at 105°, Appendix 5.8.

Assay : Protect the solutions from light throughout the assay.

Weigh accurately about 0.1 g and dissolve in 50 ml of *dimethylformamide* by swirling. Add sufficient *water* to produce 250.0 ml. Dilute 5.0 ml to 250.0 ml with *water* and mix. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 375 nm, Appendix 5.15 A. Calculate the content of $C_6H_6N_4O_4$, taking 822 as the value of E(1 per cent, 1-cm) at the maximum at about 375 nm.

Storage : Store in well-closed, light-resistant containers.

Nitrous Oxide

N_2O Mol. Wt. 44.01

Category : General anaesthetic (inhalation); analgesic.

Application : By inhalation, 60 to 80 per cent, with oxygen 20 to 40 per cent, as required.

Description : Colourless gas; odourless; tasteless.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Solubility : One volume of gas dissolves in about 1.4 volumes of *water* at 20° and at a pressure of 760 nm of mercury. Freely soluble in *alcohol*; soluble in *solvent ether* and in oils.

Standards : Nitrous Oxide contains not less than 95.0 per cent, v/v of N_2O in the gaseous phase.

NOTE – Keep the cylinder of Nitrous Oxide at a temperature between 23° and 27° for at least six hours before carrying out the following tests. The test for carbon monoxide should be carried out on the first portion of gas drawn from the cylinder and that for Nitric Oxide and nitrogen dioxide immediately thereafter. In all the tests the cylinder should be kept in the vertical position with the outlet valve uppermost when delivering the gas. In all the tests the gas should be passed at a steady rate of 4 litres per hour, unless otherwise stated, and the results should be calculated with reference to the gas at 25° and 760 torr.

Identification : (A) A glowing splinter of wood bursts into flame on contact with the gas.

(B) It is not absorbed by *alkaline pyrogallol solution.*

Acidity : To 400 ml of *water* add 0.5 ml of *methyl orange-bromocresol green solution* and boil for five minutes. Transfer 50 ml of the boiling solution to a flat-bottomed glass cylinder fitted with an inlet tube and an exit tube; the former should be of 1 mm internal diameter and should reach to 2 mm above the bottom of the cylinder; it should be immersed in the reagent to a depth of 12 to 14 cm. Transfer a further 50 ml portion to each of two comparison cylinders, labelled A and B. Add 0.2 ml of *0.01N hydrochloric acid* to cylinder A and 0.5 ml of the same reagent to cylinder B. Close the three cylinders and allow to cool. Pass 4.0 litres of the gas into the liquid in the test cylinder and transfer the liquid to a third comparison cylinder C. The colour of the liquid in C may become yellow similar to that in A, but does not become pink similar to that in B.

Alkalinity : To 400 ml of *water* add 0.5 ml of *methyl red solution* and boil for five minutes. Transfer 50 ml of the boiling solution to each of two cylinders A and B, of the type used in the test for Acidity. To cylinder B add 0.1 ml of *0.01N hydrochloric acid*, close both cylinders, allow to cool, and pass 2.0 litres of the gas into cylinder B. The colour of the solution in cylinder B indicates that its pH is not greater than that of the solution in cylinder A.

Arsine and phosphine : Through a *mercuric chloride paper* attached to a glass tube, as in the *limit test for arsenic*, Appendix 3.2.1, pass 2.0 litres. No visible stain is produced.

Carbon dioxide : Not more than 300 parts per million v/v, determined by the following method: Using cylinders of the type used in the test for Acidity, pass 1.0 litre through 50 ml of *0.3N barium hydroxide*; any turbidity produced is not more intense than that produced by adding 1 ml of a 0.11 per cent w/v solution of *sodium bicarbonate* in *carbon dioxide-free water* to 50 ml of *0.3N barium hydroxide.*

Carbon monoxide : Not more than 20 parts per million v/v determined by the following method: Connect in series a U-tube containing *silica gel* impregnated with *chromium trioxide*; a drechsel bottle containing 100 ml of a 40 per cent w/v solution of *potassium hydroxide*, a U-tube containing pellets of *potassium hydroxide*; a U-tube containing *phosphorus pentoxide*, dispersed on previously granulated, fused pumice; a tube containing *iodine pentoxide* in granules, previously dried at 200° and kept at a temperature of 120°, packed in 1-cm columns separated by 1-cm columns of glass-wool giving an effective length of 5 cm; and a flask containing 2.0 ml of *M potassium iodide* and 0.15 ml of *starch solution.*

Flush the apparatus with 5.0 litres of carbon dioxide-free air and, if necessary, discharge the blue colour in the iodide solution by adding the smaller quantity of freshly prepared *0.002N sodium thiosulphate.* Continue flushing until not more than 0.045 ml of *0.002N sodium thiosulphate* is required after passing 5.0 litres of *carbon dioxide-free air.*

Pass 5.0 litres of the sample being examined through the apparatus and flush the last traces of liberated iodine into the reaction flask by passing through the apparatus 1.0 litre of carbon monoxide-free air. Titrate the liberated iodine with *0.002N sodium thiosulphate.*

Carry out a blank determination under the same conditions, using 5.0 litres of carbon dioxide-free air. The difference between the volumes of *0.002N sodium thiosulphate* used in the two titrations is not greater than 1.0 ml.

Halogens and hydrogen sulphide : On passing 1.0 litre through 100 ml of *water* containing 1 ml of *silver nitrate solution*, neither opalescence nor darkening is produced.

Nitric oxide and nitrogen dioxide : Not more than 5 parts per million v/v in both the liquid and gaseous phases, determined by the following method: Pass the gas, at a rate of 15 litres per hour, through a solution containing 2.5 per cent w/v of *potassium permanganate* and 1.2 per cent w/v of *sulphuric acid* into evacuated gas sampling tube of 1 litre nominal capacity and fill to a pressure about 50 torr below that of the atmosphere. Calculate the volume of gas at 25° and 760 torr. Prepare solution (1) by dissolving 1 g of *sulphanilic acid* in a mixture of 10 ml of *glacial acetic acid* and 180 ml of *water.* Prepare solution (2) by dissolving 0.2 g of *N-(1-naphthyl) ethylenediamine hydrochloride* in 10 ml of a 50 per cent v/v solution of *glacial acetic acid*, heating gently and diluting to 200 ml with *water.* Mix 9 volumes of solution (1) with 1 volume of solution (2). Introduce 20 ml of this reagent mixture into the sampling tube, shake and allow to stand for ten minutes with occasional shaking. Measure the *extinction* of the resulting solution at 550 nm, Appendix 5.15 A, and correct the result to 1.0 litre of the gas at 25° and 760 torr. The *extinction* should not be greater than that of the solution obtained by adding 0.25 ml of a 0.00308 per cent w/v

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

solution of *sodium nitrite* to 20 ml of the reagent mixture.

Reducing substances : On passing the gas through 100 ml of *water* containing 0.2 ml of *0.1N potassium permanganate* the colour is not completely discharged.

Oxidising substances : On passing the gas through a freshly prepared solution of 0.5 of *soluble starch* and 0.5 g of *potassium iodide* in 100 ml of *water* containing 1 drop of *glacial acetic acid*, no colour is developed.

Water : Pass a measured quantity at a rate of 6 litres per hour through an absorption tube containing *magnesium perchlorate*; the increase in weight of the tube does not exceed 2 mg per litre of gas, the initial and final weighings of the tube being made when the air in it has been displaced by the nitrous oxide.

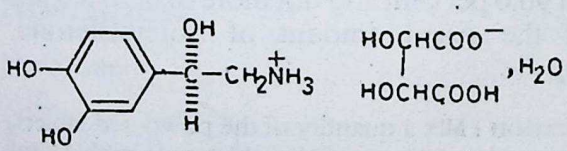
Assay : Carry out the *assay of nitrous oxide*, using 100 ml, Appendix 3.3.7.

Storage : Store under compression in metal cylinders of the type conforming to the appropriate safety regulations and at a temperature not exceeding 37°.

Labelling : The cylinder is painted blue and carries a label stating the name of the gas. In addition, the shoulder of the cylinder is labelled with the name of the gas or the symbol "N_2O" stencilled in paint.

Noradrenaline Acid Tartrate

Levarterenol Bitartrate; Norepinephrine Bitartrate



$C_8H_{11}NO_3, C_4H_6O_6, H_2O$ Mol. Wt. 337.28

Category : Adrenergic (vasopressor).

Dose : By intravenous infusion, 2 to 20 µg per minute, according to the blood pressure of the patient.

Description : White or almost white crystalline powder; odourless. It gradually darkens on exposure to air and light.

Solubility : Freely soluble in *water*; slightly soluble in *alcohol*; practically insoluble in *chloroform* and in *solvent ether*.

Standards : Noradrenaline Acid Tartrate is the monohydrate of (*R*)-[2-hydroxy-2-(3,4-dihydroxyphenyl)ethyl]ammonium hydrogen tartrate. It contains not less than 98.5 per cent and not more than the equivalent of 101.0 per cent $C_8H_{11}NO_3, C_4H_6O_6$, calculated with reference to the anhydrous substance.

Identification : (A) To 1 ml of a 1 per cent w/v solution, add one drop of *ferric chloride solution*; an intense green colour is produced. Add, drop by drop, *sodium bicarbonate solution*, the colour changes to blue and then to red.

(B) *Extinction* of a 1-cm layer of a 0.005 per cent w/v solution in *0.01N hydrochloric acid* at 279 is about 0.40, Appendix 5.15 A.

(C) To 1 ml of a 0.1 per cent w/v solution add 10 ml of *buffer solution, pH 3.6*, add 1 ml of *0.1N iodine*, set aside for five minutes and add 2 ml of *0.1N sodium thiosulphate*; not more than a faint colour is produced. Repeat the experiment, using *buffer solution, pH 6.6* instead of *buffer solution, pH 3.6*; a strong reddish violet colour is produced (distinction from Adrenaline and Isoprenaline).

(D) Dissolve 0.2 g in 2 ml of *water* containing about 10 mg of *sodium sulphite* and add sufficient *dilute ammonia solution* to give an alkaline reaction. Keep the mixture at about 4° for one hour and filter. The filtrate gives the reactions of *tartrates*, Appendix 3.1.

Melting range : Between 100° and 106°, with decomposition, Appendix 5.11.

Clarity and colour of solution : A 2.0 per cent w/v solution is clear and not more intensely coloured than a mixture of 3.0 ml of *ferric chloride C.S.*, 1.25 ml of *cobalt chloride C.S.*, 0.5 ml of *copper sulphate C.S.* and sufficient *hydrochloric acid (1 per cent w/v)* to produce 100 ml.

pH : Between 3.5 and 5.0, determined in a 1 per cent w/v solution, Appendix 5.10.

Specific optical rotation : Between −10° and −13°, determined in a 5.0 per cent w/v solution, Appendix 5.12.

Noradrenalone : *Extinction* of a 1-cm layer of a 0.2 per cent w/v solution in *0.01N hydrochloric acid* at 310 nm, is not more than 0.40, Appendix 5.15 A.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Water : Between 4.5 per cent w/w and 5.8 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately about 0.15 g, dissolve in 20 ml of *glacial acetic acid* and titrate with *0.1N perchloric acid*, using *crystal-violet solution* as indicator, to a clear blue colour. Perform a blank titration and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.03193 g of $C_8H_{11}NO_3, C_4H_6O_6$.

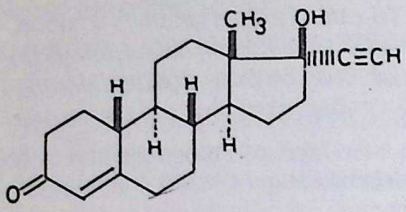
Storage : Store in tightly-closed, light-resistant containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Norethisterone

Norethindrone



$C_{20}H_{26}O_2$ Mol. Wt. 298.42

Category : Progestin.

Dose : 5 to 20 mg daily, in single or divided doses.

Description : White to creamy-white, crystalline powder; odourless.

Solubility : Practically insoluble in *water*; soluble in *chloroform*, *dioxan*, and in *pyridine*; sparingly soluble in *alcohol*; slightly soluble in *solvent ether*.

Standards : Norethisterone is 17β-hydroxy-19-nor 17α-pregn-4-en-20-yn-3-ona. It contains not less than 97.0 per cent and not more than the equivalent of 102.0 per cent of $C_{20}H_{26}O_2$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* of a 7 in 100 solution in *chloroform*, determined in a 0.1 mm cell, exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *norethisterone R.S.* similarly treated, Appendix 5.15 B.

(B) Complies with the test for *identification of steroids*, Appendix 3.3.11, using *solvent II* and *mobile phase D*.

Melting range : Between 201° and 208°, Appendix 5.11.

Specific optical rotation : Between −23° and −27°, determined in a 1.0 per cent w/v solution in *chloroform*, Appendix 5.12.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 95 volumes of *chloroform* and 5 volumes of *methyl alcohol* as the mobile phase. Apply separately to the plate 10 µl of each of three solutions in *chloroform* containing (1) 1.0 per cent w/v of the substance being examined; (2) 1.0 per cent w/v of *norethisterone R.S.*; (3) 0.01 per cent w/v of *norethisterone R.S.* After removal of the plate, allow it to dry in air until the odour of the solvent is no longer perceptible, spray with a 10 per cent v/v solution of *sulphuric acid* in *methyl alcohol*, heat at 105° for ten minutes, and examine under an ultra-violet lamp having a maximum output at about 366 nm. Any spots in the chromatogram obtained with solution (1), other than the principal spot, are not more intense than the spot in the chromatogram obtained with solution (3).

Light absorption : *Extinction* of a 1-cm layer of a 0.001 per cent w/v solution in *ethyl alcohol* at the maximum at about 240 nm, 0.55 to 0.59, Appendix 5.15 A.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g, by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately 0.2 g and dissolve in 40 ml of *tetrahydrofuran*, add 10 ml of a 10 per cent w/v solution of *silver nitrate*, and titrate with *0.1N sodium hydroxide*, determining the end-point potentiometrically. Each ml of *0.1N sodium hydroxide* is equivalent to 0.02984 g of $C_{20}H_{26}O_2$.

Storage : Preserve in tightly-closed, light-resistant containers.

Norethisterone Tablets

Norethindrone Tablets

Category : Progestin.

Dose : Norethisterone, 5 to 20 mg daily, in single or divided doses.

Usual strength : 5 mg.

Standards : Norethisterone Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Norethisterone, $C_{20}H_{26}O_2$.

Identification : Mix a quantity of the powdered tablets, equivalent to about 50 mg of Norethisterone with 15 ml of *hexane*, and stir occasionally for fifteen minutes. Centrifuge the mixture, then decant and discard the hexane. Extract the residue with two quantities, each of 10 ml of *hexane*, centrifuge and discard the washings. Add 25 ml of *chloroform* to the residue, mix by shaking for 1 to 2 minutes, and filter. Evaporate the filtrate to about 3 ml, add a few ml of *hexane* to induce crystallization and evaporate to dryness. The residue complies with the test for *identification of steroids*, Appendix 3.3.11, using *solvent II* and *mobile plase D*.

Uniformity of content : Powder one tablet and warm with about 75 ml of *ethyl alcohol* with stirring. Cool, transfer to a 100-ml volumetric flask and dilute to volume with *ethyl alcohol*. Centrifuge a few ml of the suspension until a clear supernatant liquid is obtained. Dilute 10.0 ml to 50.0 ml with *ethyl alcohol* and mix. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 240 nm, Appendix 5.15 A. Calculate

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

the content of $C_{20}H_{26}O_2$, taking 570 as the value of E(1 per cent, 1-cm) at the maximum at about 240 nm.

Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 90 per cent and 110 per cent of the average except that for one tablet the content may be between 85 per cent and 115 per cent of the average.

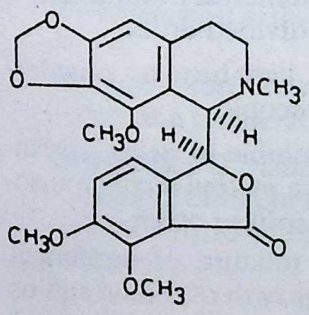
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 0.2 g Norethisterone and place in a glass column closed at the bottom with a small piece of cotton wool. The glass column consists of a piece of glass tubing about 10 mm in internal diameter and about 150 mm long, tapered at the bottom and sealed at the top to another piece of glass tubing about 25 mm in internal diameter and about 150 mm long. Place a small piece of cotton wool on top of the powder and extract with 200 ml of *light petroleum (boiling range 60° to 80°)*, discard the light petroleum. Extract the residue with about 200 ml of *chloroform*, evaporate the chloroform from the extract, and dry the residue at 105° for two hours. Allow to cool, dissolve in 40 ml of *tetrahydrofuran*, add 10 ml of a 10 per cent w/v solution of *silver nitrate*, and titrate with *0.1N sodium hydroxide*, determining the end-point potentiometrically. Each ml of *0.1N sodium hydroxide* is equivalent to 0.02984 g of $C_{20}H_{26}O_2$.

Storage : Store in well-closed, light-resistant containers.

Noscapine

Narcotine



$C_{22}H_{23}NO_7$ Mol. Wt. 413.43

Category : Antitussive.

Dose : 15 to 30 mg.

Description : Fine, almost white, crystalline powder; odourless; testeless.

Solubility : Practically insoluble in *water*; slightly soluble in *alcohol*, and in *solvent ether*; freely soluble in *chloroform*.

Standards : Noscanine is (3*S*)-6,7-dimethoxy-3-[(5*R*)-5, 6, 7, 8-tetrahydro-4-methoxy-6-methyl-1,3-dioxolo (4,5-g)-isoquinolin-5-yl] phthalide, an alkaloid obtained from opium. It contains not less than 98.5 per cent and not more than the equivalent of 101.0 per cent of $C_{22}H_{23}NO_7$, calculated with reference to the dried substance.

Identification : (A) The light absorption, in the range of 240 to 350 nm, of a 1-cm layer of a 0.006 per cent w/v solution in *alcohol* exhibits two maxima, at 291 nm and 310 nm, *extinction* at 291 nm, about 0.55 and at 310 nm about 0.7, Appendix 5.15 A.

(B) To a 0.1 g in a porcelain dish add a few drops of *sulphuric acid* and stir; a greenish-yellow solution is formed which on warming becomes red and finally violet.

(C) Dissolve 50 mg in 5 ml of *0.5N hydrochloric acid*, add 10 ml of a mixture of equal volumes of *alcohol* and a saturated solution of *sodium acetate*, mix, and allow to stand, after about three minutes, shining crystals separate.

(D) Acid solutions are dextrorotatory, solutions in *chloroform* or in *alcohol* are laevorotatory.

Melting range : Between 174° and 176°, Appendix 5.11.

Specific optical rotation : Between −196° and −201°, determined at 20° in a 4.0 per cent w/v solution in *chloroform*, Appendix 5.12.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Morphine : Dissolve 0.10 g in 10 ml of *0.1N hydrochloric acid*. To 1 ml of this solution add a mixture of 1 ml of *potassium ferricyanide solution*, 0.05 ml of *ferric chloride test-solution*, and 4 ml of *water*; no blue or dark-green colour develops within one minute.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

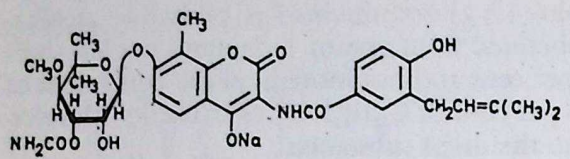
Assay : Dissolve 0.5 g in a suitable volume of *glacial acetic acid* previously neutralised to *crystal-violet solution*, warming and cooling if necessary. Titrate with *0.1N perchloric acid* to a green end-point. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.04134 g of $C_{22}H_{23}NO_7$.

Storage : Store in well-closed containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Novobiocin Sodium



$C_{31}H_{35}N_2NaO_{11}$ Mol. Wt. 634.61

Category : Antibacterial.

Dose : The equivalent of 1 to 2 g of novobiocin daily, in divided doses.

Description : White or yellowish-white crystalline powder; odourless; taste, sweet at first, becoming bitter.

Solubility : Freely soluble in *water*, in *alcohol* and in *methyl alcohol*; slightly soluble in *butyl acetate*.

Standards : Novobiocin Sodium is the monosodium salt of novobiocin, an antimicrobial substance, produced by the growth of certain strains of *Streptomyces niveus* or related organisms, or by other means. It contains not less than 850 µg of novobiocin per mg, calculated with reference to the anhydrous substance.

Identification : (A) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.001 per cent w/v solution containing 0.4 per cent w/v solution of *potassium hydroxide* exhibits a maximum only at 307 nm; the ratio of the *extinction* at 307 nm to that at 261 nm, about 3.18, Appendix 5.15 A.

(B) Ignite; the residue gives the reactions of *sodium*, Appendix 3.1.

Specific optical rotation : Between −50° and −58°, determined in a 5.0 per cent w/v solution in *methyl alcohol* containing 1 per cent v/v *hydrochloric acid*, Appendix 5.12.

pH : Between 6.6 and 8.5 determined in a 2.5 per cent w/v solution, Appendix 5.10.

Undue toxicity : Complies with the test described under Bacitracin, using 2.0 mg dissolved in 0.5 ml of *water for injection*.

Water : Not more then 6.0 per cent w/w, Appendix 3.3.25.

Assay : Carry out the *microbiological assay of antibiotics, Method A*, Appendix 4.1, and express the results in µg of novobiocin per mg. Novobiocin Sodium intended for parenteral administration complies with the following additional requirements:

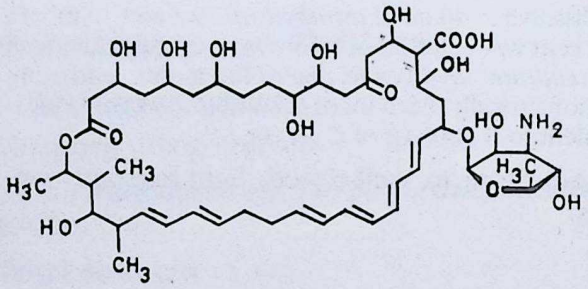
Pyrogens : Complies with the *test for pyrogens*. Appendix 2.36, using not less than 10 mg per kg of the rabbit's weight dissolved in not more than 1 ml of *saline solution*.

Sterility : Complies with the *test for sterility*, Appendix 4.6.

Storage : Store in tightly-closed, light-resistant containers, in a cool place. If it is intended for parenteral administration, the container should be sterile and sealed so as to exclude micro-organisms.

Labelling : The label on the container states (1) the date after which the contents are not intended to be used; (2) the storage conditions; (3) whether or not the contents are intended for parenteral administration.

Nystatin



Nystatin A_1

Category : Antifungal.

Dose : In the treatment of alimentary moniliasis, 1 to 2 million Units daily, in divided doses.

Description : Yellow to light-brown powder; odour, characteristic; hygroscopic.

Solubility : Very slightly soluble in *water*, sparingly soluble in *alcohol* and in *methyl alcohol*; insoluble in *chloroform* and in *solvent ether*.

Standards : Nystatin is a mixture of antifungal polyenes produced by the growth of certain strains of *Streptomyces noursei* (Fam. Streptomycetaceae) or by other means. It has a potency of not less than 4400 Units of nystatin per mg.

Identification : (A) Shake 30 mg with 5 ml of *water* for two minutes, add 2 ml of *sodium molybdotungstophosphate solution*, and allow to stand for one hour; the green colour produced is darker than that produced by repeating the test without the substance being examined.

(B) Shake 30 mg with 5 ml of *water* for two minutes, add 2 ml of a solution prepared by dissolving 0.1 g of *pyro-*

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

gallol in 100 ml of *decolourised magenta solution*, heat on a water-bath until a dark pink colour is produced, cool and allow to stand for one hour; the pink colour is retained.

Specific optical rotation : Between 0° and +25°, determined in a 1.0 per cent w/v solution in *dimethylformamide*, Appendix 5.12.

pH : Between 6.5 and 8.0, determined in 3.0 per cent w/v suspension in *water*, Appendix 5.10.

Light absorption : Dissolve 0.10 g in a mixture of 50 ml of *methyl alcohol* and 5 ml of *glacial acetic acid*, add sufficient *methyl alcohol* to produce 100.0 ml, and dilute 1.0 ml to 100.0 ml with *methyl alcohol*. The light absorption of the resulting solution, in the range 240 to 350 nm exhibits three maxima, at about 291 nm, 305 nm, and 319 nm, Appendix 5.15 A. Ratios of the *extinctions* of a 1-cm layer at the maxima at about 291 nm and 319 nm to the *extinction* at the maximum at about 305 nm, 0.61 to 0.73 and 0.83 to 0.96 respectively.

Undue toxicity : Complies with the test described under Bacitracin, using a quantity equivalent to not less than 600 Units suspended in not more than 0.5 ml of a 0.5 per cent w/v solution of *acacia* and injecting the suspension intraperitoneally.

Sulphated ash : Not more than 3.5 per cent, Appendix 3.2.7.

Loss on drying : Not more than 5.0 per cent, determined on 1.0 g by drying "in vacuo at 60°", Appendix 5.8.

Assay : Protect the solutions from light throughout the assay.

Weigh accurately about 75 mg and dissolve in sufficient *dimethylformamide* to produce 50.0 ml; dilute 10.0 ml to 200.0 ml with a solution containing 9.56 per cent w/v of *potassium dihydrogen phosphate* and 11.5 per cent v/v of *N potassium hydroxide*, and carry out the *microbiological assay of antibiotics, Method A*, Appendix 4.1.

Storage : Store in well-closed, light-resistant containers at a temperature not exceeding 5°.

Labelling : The label on the container states (1) the number of Units per mg; (2) the date after which the contents are not intended to be used; (3) the storage conditions.

Nystatin Ointment

Category : Antifungal (topical).

Usual strength : 100,000 Units per g.

Standards : Nystatin Ointment contains Nystatin in a suitable ointment base. It contains not less than 90.0 per cent and not more than 130.0 per cent of the stated number of Units of nystatin.

Identification : Boil 0.1 g with 20 ml of *methyl alcohol*, shake, cool at 10° for thirty minutes , filter and evaporate the filtrate to dryness. Dissolve the residue in 50 ml of *methyl alcohol*, 5 ml of *glacial acetic acid* and sufficient *methyl alcohol* to produce 100 ml. Dilute 25 ml to 100 ml with *methyl alcohol*. The light absorption of the resulting solution, in the range 240 to 350 nm, exhibits three maxima, at about 291 nm, 305 nm and at 319 nm, Appendix 5.15 A.

Water : Not more than 0.5 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately a quantity equivalent to 400,000 Units of nystatin, disperse in 20 ml of *solvent ether* in a stoppered flask, add 70 ml of *dimethyl formamide*, shake for 15 minutes, add 10 ml of *water*, shake vigorously for a few minutes and add sufficient *dimethyl formamide* to produce 100.0 ml. Filter and dilute 10.0 ml of the filtrate to 100.0 ml with *buffer solution, pH 6.0*. Carry out the *microbiological assay of antibiotics, Method A*, Appendix 4.1, and express the results in Units of nystatin per g.

Storage : Store in well-closed containers, in a cool place.

Labelling : The label on the container states (1) the strength in terms of Units of nystatin per g; (2) the date after which the contents are not intended to be used; (3) storage conditions.

Nystatin Tablets

Category : Antifungal.

Dose : Nystatin, 1,000,000 to 2,000,000 Units daily, in divided doses.

Usual strength : 500,000 Units.

Standards : Nystatin Tablets contain not less than 90.0 per cent and not more than 130.0 per cent of the stated number of Units of nystatin. The tablets may be coated.

Identification : Extract a quantity of the powdered tablets equivalent to 300,000 Units with a mixture of 50 ml of *methyl alcohol* and 5 ml of *glacial acetic acid*, add sufficient *methyl alcohol* to produce 100 ml and filter. Dilute 1 ml of the filtrate to 100 ml with *methyl alcohol*. The resulting solution complies with the test for *light absorption* described under Nystatin.

Disintegration : Not more than thirty minutes, using a 0.6 per cent v/v solution of *hydrochloric acid* in place of *water*; if the tablets fail to disintegrate wash them rapidly

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

by immersion in *water* and continue the test using *buffer solution, pH 6.8*, Appendix 5.6.1, the tablets are disintegrated within one hour.

Loss on drying : Not more than 5.0 per cent, determined on the powdered tablets by drying "in vacuo at 60°" for three hours, Appendix 5.8.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 200,000 Units and shake with 50 ml of *dimethylformamide* for one hour. Centrifuge, dilute 10.0 ml of the clear, supernatant liquid to 200.0 ml with a solution containing 9.56 per cent w/v of *potassium dihydrogen phosphate* and 11.5 per cent v/v of *N potassium hydroxide*, and carry out the *microbiological assay of antibiotics, Method A*, Appendix 4.1.

Storage : Store in well-closed containers, in a cool place.

Labelling : The label on the container states (1) the strength in terms of Units of nystatin; (2) the date after which the tablets are not intended to be used; (3) the storage conditions.

Nystatin Vaginal Tablets

Nystatin Pessaries

Category : Antifungal (topical)

Usual strength : 100,000 Units.

Standards : Nystatin Vaginal Tablets contain not less than 90.0 per cent and not more than 140.0 per cent of the stated number of Units of nystatin.

Identification : Comply with the **Identification** test described under Nystatin Tablets.

Disintegration : Maximum time, 60 minutes, Appendix 5.6.1.

Uniformity of weight : Weigh individually twenty tablets and determine the average weight. Not more than two of the individual weights deviate from the average weight by more than 5 per cent, and none deviates by more than 10 per cent.

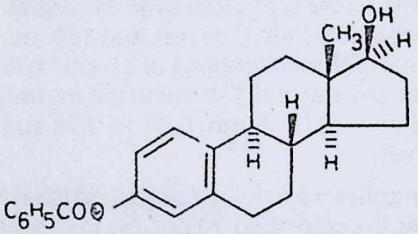
Loss on drying : Not more than 5.0 per cent, determined on 1.0 g of the powdered tablets by drying "in vacuo at 60°" for three hours, Appendix 5.8.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powdered tablets equivalent to 200,000 units of nystatin and shake with 50.0 ml of *dimethylformamide* for one hour. Centrifuge, dilute 10.0 ml of the clear, supernatant liquid to 200.0 ml with *buffer solution, pH 6.0*. Carry out the *microbiological assay of antibiotics, Method A*, Appendix 4.1.

Storage : Store in tightly-closed containers, in a cool place.

Labelling : The label on the container states (1) the strength in terms of Units of nystatin activity per tablet; (2) the date after which the tablets are not intended to be used; (3) the storage conditions.

Oestradiol Benzoate



$C_{25}H_{28}O_3$ Mol. Wt. 376.49

Category : Oestrogenic hormone.

Dose : By intramuscular injection, 1 to 5 mg daily.

Description : Colourless crystals or white crystalline powder; odourless.

Solubility : Practically insoluble in *water*, and in solutions of alkali hydroxides; slightly soluble in *alcohol*, in *acetone* and in fixed oil.

Standards : Oestradiol Benzoate is 1,3,5(10)-estratriene-3, 17β-diol 3-benzoate. It contains not less than 97.0 per cent and not more than the equivalent of 103.0 per cent of $C_{25}H_{28}O_3$, calculated with reference to the dried substance.

Identification : (A) Complies with the test for *identification of steroids*, Appendix 3.3.11, using *solvent II* and *mobile phase E* and applying to the plate 2 µl of each of the solutions.

(B) Dissolve 0.1 g in a 10 ml of *methyl alcohol* and 0.1 g of *potassium carbonate* dissolved in 0.5 ml of *water* and reflux the mixture on a water-bath for two hours. Add 30 ml of *water* and gently heat until the alcohol is evaporated. Add 15 ml of *water* and keep the solution at a temperature between 5° and 10° for one hour. Filter the precipitate, wash it with cold *water* until the washings are neutral to *litmus paper*, and dry at 105° for one hour; the Oestradiol so obtained melts at about 175°, Appendix 5.11.

(C) Evaporate the filtrate obtained in the above test to 5 ml, cool, filter if necessary and add to the filtrate 2 ml of *dilute hydrochloric acid*; a white precipitate is formed. Extract the precipitate with 5 ml of *solvent ether*, evaporate the ether and dry the residue at 60° for one hour; the

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

benzoic acid so obtained melts between 121° and 125°, Appendix 5.11.

(D) To about 1 mg add 3 drops of sulphomolybdic reagent (50 mg *ammonium molybdate* dissolved in 10 ml *sulphuric acid*). A yellowish-green colour develops. Add 1 ml of *sulphuric acid* and then 9 ml of *water*. The solution becomes pink with a yellowish fluorescence.

Melting range : Between 191° and 198°, Appendix 5.11.

Specific optical rotation : Between +57° and +63°, determined on a 1.0 per cent w/v solution in *dioxan*, Appendix 5.12.

Related foreign steroids : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 80 volumes of *benzene* and 20 volumes of *ethyl acetate* as the mobile phase. Apply separately to the plate 5 µl of each of two solutions in a mixture of 9 volumes on *chloroform* and 1 volume of *methyl alcohol* containing (1) 1.0 per cent w/v of the substance being examined and (2) 0.02 per cent w/v of the substance being examined. After removal of the plate, allow it to dry in air for five minutes, spray with a 10 per cent v/v solution of *sulphuric acid* in *alcohol* and heat at 110° for fifteen minutes. Any spot in the chromatogram obtained with solution (1), other than the principal spot is not more intense than the spot in the chromatogram obtained with solution (2).

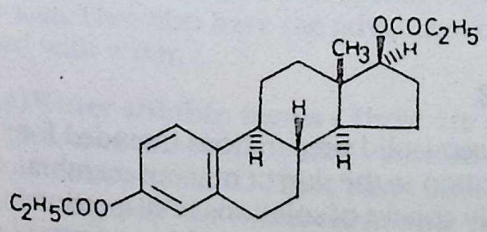
Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined by drying 1.0 g in an oven at 105° for two hours, Appendix 5.8.

Assay : Weigh accurately about 10 mg, dissolve in *alcohol* and dilute to 100.0 ml with *alcohol*. Dilute 5.0 ml of the solution to 50.0 ml with *alcohol*. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 231 nm, Appendix 5.15 A. Calculate the content of $C_{25}H_{28}O_5$, taking 490 as the value of E^{1}_{1cm} (1 per cent, 1-cm) at the maximum at about 231 nm.

Storage : Store in well-closed, light-resistant containers.

Oestradiol Dipropionate



$C_{24}H_{32}O_4$ Mol. Wt. 384.51

Category : Oestrogenic hormone.

Usual dose range : By intramuscular injection, initial, 1 to 5 mg every 1 to 2 weeks; maintenance, 1 to 2.5 mg every 10 days to 2 weeks.

Description : Colourless, white or slightly off-white crystals or a crystalline powder; odourless.

Solubility : Practically insoluble in *water* and in solutions of alkali hydroxides; slightly soluble in *alcohol*; and in vegetable oils; soluble in *acetone*, in *dioxan* and in *solvent ether*.

Standards : Oestradiol Dipropionate is 1, 3, 5(10)-estratriene-3, 17β-diol dipropionate. It contains not less than 97.0 per cent and not more than the equivalent of 103.0 per cent of $C_{24}H_{32}O_4$, calculated with reference to the dried substance.

Identification : (A) Complies with the test for *identification of steroids*, Appendix 3.3.11, using *solvent II* and *mobile phase E* and applying to the plate 2 µl of each of the solutions.

(B) Complies with **Identification** test (B) described under the Oestradiol Benzoate.

(C) Dissolve 2 mg of the Oestradiol obtained in **Identification** test (B) in 2 ml of *sulphuric acid*; the solution is greenish-yellow and exhibits a greenish fluorescence. Add to the solution one drop of *ferric ammonium sulphate solution*; the green colour is strongly intensified and on dilution with *water*, the colour changes to red or orange-red.

Melting range : Between 103° and 109°, Appendix 5.11.

Specific optical rotation : Between +35° and +41°, determined on a 1.0 per cent w/v solution in *dioxan*, Appendix 5.12.

Related foreign steroids : Carry out the test described under Oestradiol Benzoate using a mixture of 40 volumes of *benzene* and 10 volumes of *acetone* as the mobile phase.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 80°, Appendix 5.8.

Assay : Weigh accurately about 40 mg and dissolve in sufficient *methyl alcohol* to produce 100.0 ml. Dilute 10.0 ml of this solution to 100.0 ml with *methyl alcohol*. Transfer 1.0 ml to a glass-stoppered test-tube and evaporate to dryness with the aid of gentle heat and a current of air. Add 1.0 ml of *iron-phenol solution*, suspend the tube in a boiling water-bath, and heat for thirty-five minutes, immediately cool in an ice-water-bath. Remove from the ice-bath, add 10.0 ml of *dilute sulphuric acid* (1 in 3) to each tube, mix and allow to reach the room temperature. Measure the *extinction* of 1-cm layer of the resulting solution at the maximum at about 520 nm, against a blank, Appendix 5.15 A. Calculate the content of $C_{24}H_{32}O_4$, by

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

carrying out the assay simultaneously using a solution of *oestradiol dipropionate R.S.* in *methyl alcohol* and from the declared content of $C_{24}H_{32}O_4$ in *Oestradiol dipropionate R.S*

Storage : Store in well-closed, light-resistant containers.

Oestradiol Injection

Oestradiol Benzoate Injection

Category : Oestrogenic hormone.

Dose : Oestradiol Benzoate, by intramuscular injection 1 to 5 mg daily.

Usual strength : 1 mg per ml.

Standards : Oestradiol Injection is a sterile solution of Oestradiol Benzoate in Ethyl Oleate or other suitable ester, in a suitable fixed oil, or in any mixture of these; it may contain suitable alcohols. It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of $C_{25}H_{28}O_3$.

Identification : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 80 volumes of *toluene* and 20 volumes of *ethyl acetate* as the mobile phase. Apply separately to the plate 5 µl of each of the following solutions. For solution (1), add 10 ml of *trimethylpentane* to a volume of the injection equivalent to 2 mg of Oestradiol Benzoate and extract with three quantities, each of 10 ml, of *alcohol (70 per cent)*. Wash the combined extracts with 15 ml of *trimethylpentane*, evaporate the alcoholic extract to dryness and dissolve the residue in 2 ml of *chloroform*. Solution (2) is a 0.1 per cent w/v solution of *oestradiol benzoate R.S.* in *chloroform*. After removal of the plate, allow it to dry in air, spray with a 10 per cent w/v solution of *sulphuric acid* in *alcohol*, heat at 105° for ten minutes and examine under an ultra-violet lamp having a maximum output at about 366 nm. The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

Other requirements : Complies with the requirements stated under Injections.

Assay : Measure accurately a volume equivalent to about 1 mg of Oestradiol Benzoate and dissolve in 30 ml of *trimethylpentane*. Shake for two minutes with 40 ml of *alcohol (70 per cent)*, separate the alcohol layer and wash with 20 ml of *trimethylpentane*. Repeat the extraction with six quantities, each of 15 ml, of *alcohol (70 per cent)*, washing each alcohol layer with the same 20 ml of *trimethylpentane*. To the combined alcohol extracts add 5 ml of a 10 per cent w/v solution of *anhydrous sodium carbonate* and evaporate the alcohol to about 15 ml by gentle boiling in a water-bath. Cool, add 20 ml of a 10 per cent w/v solution of *sodium hydroxide*, transfer to a separator with the aid of *water* and extract for two minutes with 30 ml of *trimethylpentane*. Wash the *trimethylpentane* with four quantities, each of 5 ml, of a 10 per cent w/v solution of *sodium hydroxide*. Combine the alkaline layers and acidify with *sulphuric acid (50 per cent v/v)*, cool, and shake for two minutes with two successive quantities, each of 20 ml, of *benzene*, washing each benzene layer in succession with the same two quantities each of 5 ml of a 10 per cent w/v solution of *anhydrous sodium carbonate* and two quantities each of 5 ml of *water*. Clarify the benzene layer with *anhydrous sodium sulphate*, combine and dilute to 50 ml with benzene. Evaporate 2 ml in a test-tube until ebullition just stops, instantly remove the tube dry, place in a vacuum desiccator, and evacuate continuously for one hour. Add 1 ml of *iron-phenol solution*; stopper the tube and set aside for thirty minutes shaking frequently. Heat in a water-bath for thirty-five minutes, shaking for a few seconds after the first five minutes. Cool in ice for two minutes, add 4 ml of a mixture of 35 volumes of *sulphuric acid* and 65 volumes of *water*. Set aside for five minutes, mix thoroughly and measure the *extinction* at the maximum at about 520 nm and at 420 nm, Appendix 5.15 A, using as a blank 1 ml of *iron-phenol solution* treated as described above, commencing at the words "stopper the tube.....". Repeat the determination using a solution of 1 mg of *oestradiol benzoate* in 5 ml of *benzene* in place of oestradiol benzoate injection. Determine the weight in mg of oestradiol benzoate in the volume of injection taken by the formula A/B, where A and B are the difference between the *extinction* at the maximum at about 520 nm and half the *extinction* at 420 nm for the first and second determinations respectively (Lubricants other than *water* should not be used on the stopcocks of the separators).

Storage : Store in single-dose or multiple-dose, light-resistant containers.

Labelling : The lebel on the container states (1) the composition of the solvent; (2) "For intramuscular injection only"; (3) that any solid matter that has separated on standing should be redissolved by warming before use.

Ointments

Ointments are semisolid preparations intended for external application to the skin or mucous membranes. They usually consist of solutions or dispersions of one or more medicaments in suitable non-aqueous bases. Ointments are so formulated that the preparation is essentially immiscible with the skin

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

secretion. They are used as emollients and for applying medicaments to the skin for protective, therapeutic or prophylactic purposes where a degree of occlusion is desired. They may contain suitable antimicrobial preservatives.

In choosing an ointment base several factors such as the action desired, nature of the medicament to be incorporated, stability and so on are to be considered. Ideally, an ointment base should not produce irritation or sensitization of the skin, nor should it retard wound healing, it should be smooth, inert, odourless, physically and chemically stable and compatible with the skin and with the incorporated medicaments. It should be of such consistency that it spreads and softens when stress is applied.

Ointment bases are often anhydrous and comprise fats, oils or waxes of animal, vegetable or mineral origin. They fall into four general classes:

(1) Fatty bases : These are usually anhydrous and may contain water-insoluble hydrocarbons, vegetable oils, animal fats and waxes, silicones or certain synthetic esters. They serve to keep the medicaments in prolonged contact with the skin and act as occlusive dressings. They have a low capacity to absorb water and are used chiefly for their emollient effects. They do not 'dry out' or change noticeably on ageing. They are also difficult to wash off.

(2) Absorption bases : These have a capacity to absorb water; they typically consist of a hydrophillic fatty base in which a water-in-oil emulsion can be incorporated to render them hydrophilic or of water-in-oil emulsions that permit the incorporation of additional quantities of aqueous solutions. Bases of this type are used as vehicles for aqueous liquids or solutions of medicaments.

(3) Water-removable bases : Such bases are oil-in-water emulsion and are often called "creams". They are also described as "water-washable" as they can be easily washed from the skin or clothing, with water. They also have the advantage of being diluted with water.

(4) Water-soluble bases : These are the so-called "greaseless ointment bases" consisting of water-soluble constituents. These bases offer many of the advantages of the water-removable bases and, in addition, contain no water-insoluble substances such as paraffins, waxes, etc. They may in some cases be irritating to inflamed tissue.

General Requirements

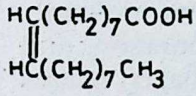
1. Ointments should be homogenous, smooth and free from lumps.

2. Ointments should be supplied in suitable containers fitted with a closure which minimises contamination with miero-organisms. There should be no leakage of the ointment from the containers or through the closures.

Storage : Ointments should be stored in a cool place.

Labelling : The label on the container states the storage conditions.

Oleic Acid



$C_{18}H_{34}O_2$ Mol. Wt. 282.47

Category : Pharmaceutical aid (emulsion adjuvant).

Description : Colourless or yellowish to pale brown, oily liquid; odour and taste characteristic. On exposure to air it darkens in colour, and the odour and taste become more pronounced.

Solubility : Practically insoluble in *water*; readily soluble in *alcohol*, in *chloroform* and in *solvent ether*.

Standards : Oleic acid is obtained from fats or fixed oils and consists chiefly of (*Z*)-9-octadecenoic acid, $C_{17}H_{33} \cdot COOH$.

Wt. per ml : Between 0.889 g and 0.895 g, Appendix 5.19.

Acid value : Between 195 and 204, Appendix 3.3.15.

Iodine value : Between 85 and 95, Appendix 3.3.18.

Mineral acids : Shake 5 ml with an equal volume of *water*, allow to separate, and filter through paper moistened with *water*; the filtrate is not acidic to *methyl orange solution*.

Neutral fats and mineral oils : Boil 1 ml with 5 ml of *N sodium carbonate* and 25 ml of *water* in a large flask; the solution, while hot, is clear, or at most opalescent.

Congealing point : Dry about 10 ml by heating at 110° with frequent stirring, transfer to a test-tube about 20 mm in diameter, cool, and when at 15°, immerse the tube in a suitable water-bath, so that the cooling takes place at the

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

rate of about 2° per minute. Stir the sample with a thermometer; it does not become cloudy until the temperature has fallen to 10°; on further cooling it congeals to a white solid or semi-solid mass at about 4°.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Storage : Store in well-filled, tightly-closed, light-resistant containers.

Opium

Raw Opium

Category : Hypnotic; sedative; narcotic; analgesic.

Dose : 25 to 200 mg.

Standards : Opium is the latex obtained by incision from the unripe capsule of *Papaver somniferum* Linn. (Fam. Papaveraceae), dried or partly dried by heat or spontaneous evaporation, and worked into somewhat irregularly shaped masses (natural opium) or moulded into masses of more uniform size and shape (manipulated opium). It contains not less than 9.5 per cent of morphine, calculated as anhydrous morphine.

Description : odour, strong and characteristic; taste, bitter.

Macroscopical—Usually occurs in roughly cubical to irregularly-shaped pieces or soft masses weighing about 900 g and wrapped in plastic material; internally dark brown, smooth and homogeneous.

Microscopical—In the residue left after removing the amorphous latex by exhaustion with *water* the following structures are usually to be found: poppy capsule represented by occasional fragments of epidermis composed of small 5 to 6-sided cells with strongly thickened walls and sometimes with stellate lumina; stomata infrequent, anomocytic, 17 µm wide and 25 µm long or sometimes circular. Pollen grains occasional, sub-spherical, with 3 pores, 16-20 to 30-40 µm in diameter.

Assay : Weigh accurately 8 g, and triturate in a mortar with 10 ml of *water* until a perfectly uniform mixture is produced. Add a further 20 ml of *water* and 2 g of *calcium hydroxide* and mix very thoroughly. Transfer the mixture to a tared flask rinsing the mortar with successive small quantities of *water* sufficient to produce 90 g. Stopper the flask, and shake occasionally during half an hour. Filter, and collect 52 ml of the filtrate, representing 5 g of the opium being assayed. Transfer to a small conical flask, add 5 ml of *alcohol (90 per cent)* and 25 ml of *solvent ether*, stopper the flask, shake, add 2.0 g of *ammonium chloride*, shake for five minutes and then occasionally during half an hour, making the total time of shaking about fifteen minutes. Allow to stand overnight. Decant the ethereal layer as completely as possible into a funnel, fitted with a tightly packed plug of cotton wool, rinse the flask and its contents with a further 10 ml of *solvent ether*, and again decant through the filter. Wash the filter with 5 ml of *solvent ether*, added slowly and in portions and pour the aqueous liquid into the filter, without attempting to remove all the crystals. When all the liquid has passed through, wash the flask and filter with *morphinated water*, until the filtrate is free from chloride. Wash the crystals on the filter back into the flask, add 30.0 ml of *0.1N sulphuric acid*, boil, cool, and titrate the excess of acid with *0.1N sodium hydroxide*, using *methyl red solution* as indicator. Each ml of *0.1N sulphuric acid* is equivalent to 0.02853 g of anhydrous morphine. To the amount indicated by the titration add 0.052 g in order to correct for loss of morphine due to its solubility.

Storage : Store in well-closed, containers.

OPIUM POWDER

Standards : Opium Powder is Opium, dried at a temperature not exceeding 70°, and reduced to a *fine* or *moderately fine* powder, and adjusted by the addition of powdered Lactose suitably coloured with burnt sugar, or of other suitable diluent, to contain not less than 9.5 per cent and not more than 10.5 per cent of morphine, calculated as anhydrous morphine.

Description : A light brown powder, consisting of yellowish-brown or brownish-red particles. Odour and taste, characteristic of Opium.

Microscopical—The residue left after extraction with *water* exhibits the structures described under Opium, and if powdered cocoa husk is present, the following: brown colour of the fragments; narrow spiral vessels about 10 to 20 microns wide, in groups of from one to six, traversing a spongy parenchyma of thin-walled cells about 40 to 60 microns in either direction and united by arm-like projection enclosing almost circular intercellular spaces; fragments of the sclerenchymatous layer, consisting of thick-walled lignified brown, rectangular to polyhedral cells in a single layer, individual cells about 5 to 10 microns wide and 10 to 30 microns long; fragments of mucilage staining in *ruthenium red solution*.

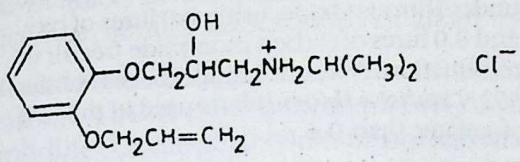
Assay : Carry out the **Assay** described under Opium.

Storage : Store in well-closed, containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Oxprenolol Hydrochloride



$C_{15}H_{23}NO_3, HCl$ Mol. Wt. 301.81

Category : Beta-adrenergic receptor blocking agent.

Dose : 40 mg to 2 g daily, in divided doses.

Description : White to slightly cream-coloured, crystalline powder; almost odourless.

Solubility : Very soluble in *water*; freely soluble in *alcohol*; very slightly soluble in *solvent ether*.

Standards : Oxprenolol Hydrochloride is *N*-[3-(2-allyloxyphenoxy)-2-hydroxypropyl]-*N*-isopropylammonium chloride. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_{15}H_{23}NO_3, HCl$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *oxprenolol hydrochloride R.S.*, Appendix 5.15 B.

(B) The light absorption in the range 230 to 350 nm, of a 1-cm layer of a 0.008 per cent w/v solution in *0.01N hydrochloric acid* exhibits a maximum only at 273 nm; *extinction* at 273 nm, about 0.6, Appendix 5.15 A.

(C) Dissolve 0.2 g in 10 ml of *water*, make alkaline with *dilute sodium hydroxide solution* and extract with two quantities, each of 5 ml of *solvent ether*. Wash the combined extracts with *water* until the washings are free from alkali, shake with *anhydrous sodium sulphate*, filter and evaporate the filtrate to dryness. The residue melts at about 76°, Appendix 5.11.

(D) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

Melting range : Between 106° and 109°, Appendix 5.11.

pH : Between 4.0 and 6.0, determined in a 5.0 per cent w/v solution, Appendix 5.10.

Heavy metals : Not more than 20 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

Foreign substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel HF 254* as coating substance and mixture of 90 volumes of *chloroform* and 10 volumes of *methyl alcohol* as the mobile phase. Keep a beaker containing *strong ammonia solution* in the tank and allow the solvent front to ascend 10 cm above the line of application. Apply separately to the plate 5 µl of each of three solutions containing (1) 2.0 per cent of the substance being examined, (2) 0.01 per cent w/v of *1-(3-allyl-2-hydroxyphenoxy)-3-isopropylaminopropan-2-ol hydrochloride R.S.* and (3) 0.01 per cent w/v of *1-(2-hydroxyphenoxy)-3-isopropylaminopropan-2-ol hydrochloride R.S.* After removal of the plate, dry at 40° for ten minutes, allow to cool, and spray with a freshly prepared solution of 5.6 per cent w/v *potassium ferricyanide* and 6.0 per cent w/v of *ferric chloride*. Any spots in the chromatogram obtained with solution (1), other than the principal spot are not more intense than the proximate spots in the chromatogram obtained with solutions (2) and (3).

Sulphapted ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.4 g and dissolve in 50 ml of *glacial acetic acid*. Add 10 ml of *mercuric acetate solution* and titrate with *0.1N perchloric acid* using *1-naphtholbenzein solution* as indicator. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.03018 g of $C_{15}H_{23}NO_3, HCl$.

Storage : Store in well-closed containers.

Oxprenolol Tablets

Category : Beta-adrenergic receptor blocking agent.

Dose : Oxprenolol Hydrochloride, 40 mg to 2 g daily, in divided doses.

Usual strengths : 40 mg and 80 mg.

Standards : Oxprenolol Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Oxprenolol Hydrochloride, $C_{15}H_{23}NO_3, HCl$. The tablets may be coated.

Identification : (A) To a quantity of the powdered tablets equivalent to 50 mg of Oxprenolol Hydrochloride add 10 ml of *water* and 2 ml of *dilute sodium hydroxide solution* and extract with 10 ml of *chloroform*. Filter the chloroform extract and evaporate the filtrate to dryness. The *infra-red absorption spectrum* of the residue exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *oxprenolol hydrochloride R.S.*, Appendix 5.15 B.

(B) The residue obtained in **Identification** test (A) melts at about 76°, Appendix 5.11.

(C) The aqueous layer obtained in **Identification** test (A) gives the reactions of *chlorides*, Appendix 3.1.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Foreign substances : Comply with the test described under Oxprenolol Hydrochloride using as solution (1) the supernatant liquid obtained by extracting a quantity of the powdered tablets equivalent to 100 mg of Oxprenolol Hydrochloride with 10 ml of *water* and centrifuging.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 20 mg of Oxprenolol Hydrochloride, add 20 ml of *water*, 25 ml of *methylene chloride* and 2 ml of *sodium hydroxide solution*. Shake for one minutes, allow to separate and extract the aqueous layer with three further quantities, each of 25 ml of *methylene chloride*. Wash the combined extracts with 5 ml of *water* and evaporate almost to dryness on a water-bath, removing the last traces of solvent in a current of air. Dissolve the residue in 25 ml of *0.1N hydrochloric acid*, add sufficient *water* to produce 250.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 273 nm, Appendix 5.15 A. Calculate the content of $C_{15}H_{23}NO_3$, HCl, taking 74.5 as the value of E(1 per cent, 1-cm) at the maximum at about 273 nm.

Storage : Store in tightly-closed containers.

Oxygen

O_2 Mol. Wt. 32.00

Category : Medicinal gas.

Description : Colourless gas; odourless and tasteless.

Solubility : At 20° and a pressure of 700 torr, 1 volume dissolves in about 32 volumes of *water* and in about 3.5 volumes of *alcohol*.

Standards : Oxygen contains not less than 99.0 per cent v/v of O_2.

NOTE—Keep the cylinder of Oxygen at a temperature between 23° and 27° for at least six hours before carrying out the following tests: In all the tests the gas should be passed at a steady rate of 4 litres per hour and the results should be calculated with reference to the gas at 25° and 760 torr.

Identification : (A) It causes a glowing splinter to burn with a flame.

(B) It is absorbed when shaken with *alkaline pyrogallol solution*, the solution becoming dark brown.

(C) When mixed with an equal volume of *nitric oxide*, red fumes are produced (distinction from nitrous oxide).

Acidity and Alkalinity : Complies with the tests described under Nitrous Oxide.

Carbon monoxide : Not more than 5 parts per million v/v, determined by the following method: Carry out the test described under Nitrous Oxide, using 8.0 litres of oxygen in the test and 8.0 litres of carbon monoxide-free air in the blank determination. The difference between the volumes of *0.002N sodium thiosulphate* used in the two titrations is not greater than 0.4 ml.

Carbon dioxide : Not more than 30 parts per million v/v, determined by the method described under Nitrous Oxide.

Halogens : Pass a volume equivalent to 2.0 litres measured at 25° and 760 torr through a mixture of 100 ml of *water* and 1 ml of *silver nitrate solution*; no opalescence is produced.

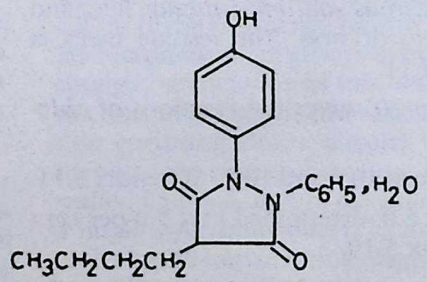
Oxidising substances : Pass a volume equivalent to 2.0 litres, measured at 25° and 760 torr through a freshly prepared solution of 0.5 g of *soluble starch* and 0.5 g of *potassium iodide* in 100 ml of *water* containing 1 drop of *glacial acetic acid*; the colour of the liquid is not changed.

Assay : Carry out the *assay of oxygen*, using 100 ml, Appendix 3.3.8.

Storage : Store under compression in metal cylinders of the type conforming to the appropriate safety regulations. Valves should not be lubricated with oil or grease.

Labelling : The shoulder of the metal cylinder is painted white and the remainder is painted black. The cylinder carries a label stating the name of the gas and in addition, the name of the gas or the symbol "O_2" is stencilled in paint on the shoulder.

Oxyphenbutazone



$C_{19}H_{20}N_2O_3, H_2O$ Mol. Wt. 342.39

Category : Anti-inflammatory (non-steroid); analgesic.

Dose : 200 to 400 mg daily, in divided doses.

Description : White to yellowish-white, crystalline powder; almost odourless; taste, bitter.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Solubility : Practically insoluble in *water*, soluble in *alcohol*, in *chloroform*, in *solvent ether* and in *acetone*; soluble in solutions of alkali hydroxides.

Standards : Oxyphenbutazone is the monohydrate of 4-butyl-2-(4-hydroxyphenyl)-1-phenylpyrazolidine-3,5-dione. It contains not less than 98.0 per cent and not more than the equivalent of 100.5 per cent of $C_{19}H_{20}N_2O_3$, calculated with reference to the anhydrous substance.

Identification : (A) To 0.1 g add 1 ml of *glacial acetic acid* and 2 ml of *hydrochloric acid* and heat on a water-bath for thirty minutes, cool, add 10 ml of *water* and filter. To the filtrate add 3 ml of *0.1M sodium nitrite*; a yellow colour is produced. Add 1 ml of the solution to 5 ml of *β-naphthol solution*; a brownish-red precipitate is formed which dissolves on the addition of *alcohol* yielding a red solution.

(B) The light absorption, in the range 230 to 350 nm of a 1-cm layer of a 0.001 per cent w/v solution in *0.01M sodium hydroxide* exhibits a maximum only at 254 nm; *extinction* at 254 nm is about 0.75, Appendix 5.15 A.

Clarity and colour of solution : To 0.5 g add a mixture of 12 ml of *N sodium hydroxide* and 8 ml of a 7.5 per cent w/v solution of *aminoacetic acid*, shake for one minute and maintain at 25° for exactly one hour. The solution is clear and the *extinction* of a 1-cm layer at 420 nm is not more than 0.10, Appendix 5.15 A.

Heavy metals : Not more than 10 parts per million, determined on 2.0 g by Method B, Appendix 3.2.4.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Water : Between 5.0 per cent and 6.0 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately about 0.5 g, dissolve in 25 ml of *acetone* and titrate with *0.1N sodium hydroxide*, using *bromothymol blue solution* as indicator and continuing the titration until the blue colour persists for at least thirty seconds. Repeat the operation without the substance being examined, the difference between the titration represents the amount of alkali required by the oxyphenbutazone. Each ml of *0.1N sodium hydroxide* is equivalent to 0.03244 g of $C_{19}H_{20}N_2O_3$.

Storage : Store in tightly-closed, containers.

Oxyphenbutazone Tablets

Category : Anti-inflammatory (non-steroid)

Dose : Oxyphenbutazone, 200 to 400 mg daily, in divided doses.

Usual strength : 100 mg.

Standards : Oxyphenbutazone Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Oxyphenbutazone, $C_{19}H_{20}N_2O_3, H_2O$. The tablets are coated.

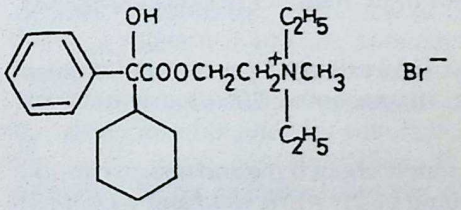
Identification : Extract a quantity of the powdered tablets equivalent to about 0.1 g of Oxyphenbutazone with 20 ml of *acetone*, filter, and evaporate the filtrate to dryness. The residue complies with **Identification** tests (A) and (B) described under Oxyphenbutazone.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powdered tablets equivalent to about 0.5 g of Oxyphenbutazone and extract with 30, 10 and 10 ml of warm *acetone*. Filter the combined extracts, cool, and complete the **Assay** described under Oxyphenbutazone, beginning at the words "titrate with *0.1N sodium hydroxide*.....". Each ml of *0.1N sodium hydroxide* is equivalent to 0.03424 g of $C_{19}H_{20}N_2O_3, H_2O$.

Storage : Store in tightly-closed containers.

Oxyphenonium Bromide



$C_{21}H_{34}BrNO_3$ Mol. Wt. 428.47

Category : Anticholinergic.

Dose : 5 to 10 mg.

Description : White, crystalline powder; odourless.

Solubility : Soluble in *water*, in *methyl alcohol*, in *alcohol* and in *glacial acetic acid*; slightly soluble in *acetone*; practically insoluble in *solvent ether*.

Standards : Oxyphenonium Bromide is *N*[2-(2-cyclohexyl)-2-hydroxyglycoloyloxy ethyl]-*N*-*N*-diethylmethylammonium bromide. It contains not less than 99.0 per cent of $C_{21}H_{34}BrNO_3$, calculated with reference to the dried substance.

Identification : (A) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using a suitable silica gel as the coating substance and a mixture of 7 volumes of *n-butyl-alcohol*, 2 volumes of *formic acid* and one

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

volume of *water* as the mobile phase. Apply separately to the plate 5 µl of each of two solutions in *methyl alcohol* containing (1) 2 per cent w/v of the substance being examined and (2) *oxyphenonium bromide R.S.* respectively. Develop the chromatogram until the solvent front is 10 to 12 cm above the starting line. Allow the plate to dry in air and spray with a 20 per cent v/v solution of *sulphuric acid* in *methyl alcohol*. The principal spot in the chromatogram obtained with solution (1) corresponds in colour and intensity with that obtained with solution (2)

(B) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.05 per cent w/v solution in *aldehyde-free alcohol* exhibits maxima at 252 nm, 258 nm and 264.5 nm, Appendix 5.15 A.

Melting range : Between 189° and 194°, Appendix 5.11.

Arsenic : Not more than 2 parts per million, Appendix 3.2.1.

Heavy metals : Not more than 10 parts per million, determined by Method A in a solution prepared in the following manner: Ignite 2 g with 8 g of *magnesium nitrate*, cool, add 6 ml of 60 per cent w/w *nitric acid* and heat at about 800° until a white residue is obtained. Dissolve the residue in 20 ml of *dilute acetic acid Sp.* Filter, if necessary, Appendix 3.2.4.

Sulphate : Dissolve 0.5 g in 10 ml of *water*, add 2 ml of *N hydrochloric acid* and 2 ml of *barium chloride solution*. Heat to boiling. The solution does not turn opalescent.

Sulphated ash : Not more than 0.5 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1 g by drying "in vacuo at 70°" for five hours, Appendix 5.8.

Assay : Weigh accurately about 0.8 g and dissolve in 100 ml of *water*. Add 10 ml of *2N nitric acid* and 25.0 ml of *0.1N silver nitrate*. Titrate with *0.1N ammonium thiocyanate*, using *ferric ammonium sulphate solution* as indicator and shaking vigorously as the end-point is approached. Each ml of *0.1N silver nitrate* is equivalent to 0.04284 g of $C_{21}H_{34}BrNO_3$.

Storage : Store in well-closed, light-resistant containers in a cool place.

Oxyphenonium Bromide Tablets

Category : Anticholinergic.

Dose : Oxyphenonium Bromide, 5 to 10 mg.

Usual strength : 5 mg.

Standards : Oxyphenonium Bromide Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Oxyphenonium Bromide, $C_{21}H_{34}BrNO_3$.

Identification : Triturate a quantity of the powdered tablets equivalent to about 50 mg of Oxyphenonium Bromide with 5 ml of *water* and centrifuge. To the supernatant liquid add 10 ml of saturated solution of *picric acid*. Keep aside for an hour. The crystals after washing first with 5 ml of *water* and then with 0.5 ml of *ethyl alcohol* followed by 5 ml of *solvent ether* and drying "in vacuo at 70°", melt at about 102°, Appendix 5.11.

Uniformity of content : Finely crush one tablet, shake for thirty minutes with 20.0 ml of *water* and centrifuge. Pipette 10 ml of the clear supernatant liquid into a separating funnel, add 10 ml of *cobalt thiocyanate solution* and extract with two successive quantities, each of 10 ml of *benzene*. Combine the extracts in a 25-ml volumetric flask and make up to volume with *benzene*. Add a few grams of *anhydrous sodium sulphate* to clarify the solution. Measure the *extinction* of a 2-cm layer of the resulting solution at the maximum at about 620 nm, Appendix 5.15 A, using *benzene* as the blank. Calculate the content of $C_{21}H_{34}BrNO_3$ from the *extinction* obtained in the **Assay** with the solution of *oxyphenonium bromide R.S.* Repeat the operation using a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 85 and 115 per cent of the average except that for one tablet the content may be between 80 and 120 per cent of the average.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and finely powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 20 mg of Oxyphenonium Bromide and shake with 40 ml of *water* for thirty minutes in a 50-ml volumetric flask. Make up to volume with *water*, mix and centrifuge. Pipette 25 ml of the supernatant liquid into a separating funnel and add 20 ml of *cobalt thiocyanate solution*. Extract with two successive quantities, each of 25 ml, of *benzene*. Combine the extracts in a 50-ml volumetric flask and make upto volume with *benzene*. Add a few grams of *anhydrous sodium sulphate* to clarify the solution. Measure the *extinction* of a 1-cm layer at the maximum at about 620 nm, Appendix 5.15 A, using *benzene* as the blank. Calculate the content of $C_{21}H_{34}BrNO_3$ from the *extinction* obtained by repeating the operation using 25.0 ml of a 0.04 per cent w/v solution of *oxyphenonium bromide R.S.* and beginning at the words "add 20 ml of *cobalt thiocyanate solution*....." and from the declared content of $C_{21}H_{34}BrNO_3$ in *oxyphenonium bromide R.S.*

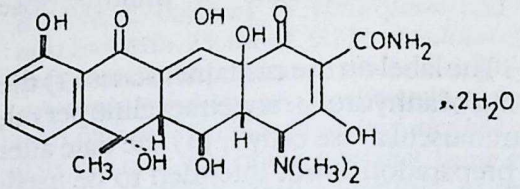
Storage : Store in light-resistant containers, in a cool place.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Oxytetracycline

Oxytetracycline Dihydrate



$C_{22}H_{24}N_2O_9,2H_2O$ Mol. Wt. 496.47

Category : Antibacterial.

Dose : 1 to 2 g daily, in divided doses.

Description : Tan yellow, or light yellow (with or without a greenish tinge), crystalline powder; odourless; taste, slightly bitter.

Solubility : Very slightly soluble in *water*; sparingly soluble in *alcohol*; freely soluble in *dilute hydrochloric acid* and in solutions of alkali hydroxides.

Standards : Oxytetracycline is the dihydrate of (4*S*, 4a*R*, 5*S*, 5a*R*, 6*S*, 12a*S*)-4-dimethylamino-1, 4, 4a, 5, 5a, 6, 11, 12a-octahydro-3, 5, 6, 10, 12, 12a-hexahydroxy-6-methyl-1, 11-dioxonaphthacene-2-carboxamide, a substance produced by the growth of certain strains of *Streptomyces rimosus*, or obtained by any other means. It contains not less than 900 µg of $C_{22}H_{24}N_2O_9$ per mg, calculated with reference to the anhydrous substance.

Identification : (A) Complies with **Identification** test (A) described under Oxytetracycline Hydrochloride, using as solution (2) a 0.05 per cent w/v solution of *oxytetracycline R.S.* in *methyl alcohol* and as solution (3) a solution in *methyl alcohol* containing 0.05 per cent w/v of *demethylchlortetracycline hydrochloride R.S.*, 0.05 per cent w/v of *oxytetracycline R.S.* and 0.05 per cent w/v of *tetracycline hydrochloride R.S.*

(B) To 0.5 mg add 2 ml of *sulphuric acid*; a red colour is produced; on adding 1 ml of *water* the colour changes to yellow to tan yellow.

(C) Dissolve about 2 mg in 5 ml of a 1 per cent w/v solution of *sodium carbonate* and 2 ml of *diazotised sulphanilic acid solution*; an orange-red to brownish-red colour is produced.

Specific optical rotation : Between –203° and –216°, determined at 20° in a 1 per cent w/v solution in *0.1N hydrochloric acid*, Appendix 5.12.

Light absorption : *Extinction* of a 1-cm layer of a 0.002 per cent w/v solution in *buffer solution, pH 2.0* at the maximum at about 353 nm, 0.54 to 0.58, Appendix 5.15 A.

Light absorbing impurities : *Extinction* at 430 nm, of a 1-cm layer of a 0.2 per cent w/v solution in a mixture of 1 volume of *N hydrochloric acid* and 99 volumes of *methyl alcohol*, not more than 0.25. *Extinction* at 490 nm of a 1-cm layer of a 1.0 per cent w/v solution in the same solvent, not more than 0.20, Appendix 5.15 A. Make the measurement within one hour of the preparation of the solutions.

pH : Between 5.0 and 7.5, determined in a 1 per cent w/v suspension in freshly boiled and cooled *water*, Appendix 5.10.

Undue toxicity : Complies with the test described under Bacitracin, the dose being 0.5 ml of a solution containing the equivalent of 2 mg of oxytetracycline per ml, prepared by dissolving a quantity equivalent to 40 mg of oxytetracycline in 2 ml of *0.1N hydrochloric acid* and diluting to 20 ml with *water for injection*.

Water : Between 6.0 per cent and 9.0 per cent w/w, Appendix 3.3.25.

Assay : Use either of the following methods; however the results obtained from the microbiological assay shall be official.

(1) Weigh accurately about 50 mg, dissolve in 25 ml of *0.1N hydrochloric acid* and add sufficient *water* to produce 250.0 ml. Pipette 10 ml into a test-tube, and 10.0 ml of a 0.05 per cent w/v solution of *ferric chloride* in a mixture of 10 volumes of *0.1N hydrochloric acid* and 90 volumes of *water*. Mix and allow to stand for fifteen minutes. Measure the *extinction* of a 1-cm layer of the resulting solution at 490 nm, Appendix 5.15 A, using as a blank 10.0 ml of *0.1N hydrochloric acid* treated in the same manner. Calculate the content of $C_{22}H_{24}N_2O_9$ from the *extinction* obtained by simultaneously carrying out the assay, using *oxytetracycline R.S.* instead of the substance being examined and the declared content of $C_{22}H_{24}N_2O_9$ in *oxytetracycline R.S.*

(2) Carry out the *microbiological assay of antibiotics, Method A or B*, Appendix 4.1, and express the result in µg of oxytetracycline, $C_{22}H_{24}N_2O_9$ per mg.

Oxytetracycline intended for parenteral administration complies with the following additional requirements:

Histamine-like substances : Complies with the *test for histamine-like substances*, Appendix 2.35, the dose being 0.6 ml per kg of the cat's weight, of a solution containing the equivalent of 5 mg of oxytetracycline per ml, prepared by dissolving a quantity equivalent to 40 mg of oxytetracycline in 2 ml of *0.1N hydrochloric acid* and diluting to 8 ml with *water for injection*.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using 1 ml per kg of the rabbit's weight of a solution containing the equivalent of 40 mg of oxytetracycline dissolved in 2 ml of *0.1N hydrochloric acid* and sufficient *water for injection* to produce 8 ml.

Storage : Store in tightly-closed, light-resistant containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Labelling : The label on the container states (1) the date after which the contents are not intended to be used; (2) the storage conditions; (3) whether or not the contents are intended for parenteral administration.

Oxytetracycline Injection

Category : Antibiotic.

Dose : Oxytetracycline, by intramuscular injection 200 to 500 mg daily, in divided doses.

Usual strengths : 50 mg per ml; 125 mg per ml.

Standards : Oxytetracycline Injection is a sterile solution of Oxytetracycline with or without one or more suitable buffer substances, anaesthetics, preservative, anti-oxidants, complexing agents and solvents in Water for Injection. It contains not less than 90.0 per cent and not more than 120.0 per cent of the stated amount of anhydrous oxytetracycline, $C_{22}H_{24}N_2O_9$.

Description : Clear yellow to tan yellow solution. It may have a greenish tinge.

Identification : (A) Complies with **Identification** test (A) described under Doxycycline Hydrochloride, using as solution (1) a solution prepared by shaking a quantity equivalent to 10 mg of anhydrous oxytetracycline with 20 ml of *methyl alcohol*, centrifuging if necessary and using the clear supernatant liquid; solution (2) is a freshly prepared 0.05 per cent w/v solution of *oxytetracycline dihydrate R.S.* in *methyl alcohol.*

(B) To 0.1 ml add 2 ml of *sulphuric acid*; a deep crimson colour is produced. Add 1 ml of *water*; the colour changes to yellow.

pH : Between 8.0 and 9.0, Appendix 5.10.

Histamine-like substances : Complies with the *test for histamine-like substances*, Appendix 2.35, the dose being 0.6 ml per kg of the cat's weight of a solution containing the equivalent of 5 mg of oxytetracycline per ml.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using 1 ml per kg of the rabbit's weight of a solution containing the equivalent of 5 mg of oxytetracycline per ml.

Undue toxicity : Complies with the test for **Undue toxicity** described under Bacitracin, the dose being 0.5 ml of a solution containing the equivalent of 2 mg of oxytetracycline per ml injected intraperitoneally.

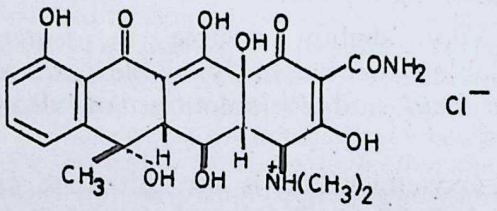
Other requirements : Complies with the requirements stated under Injections.

Assay : Carry out the *microbiological assay of antibiotics, Method A* or *B*, Appendix 4.1, and express the result in mg of oxytetracycline $C_{22}H_{24}N_2O_9$ per ml.

Storage : Store in single-dose or multiple-dose containers.

Labelling : The label on the container states (1) the strength in mg of anhydrous oxytetracycline per ml; (2) "for intramuscular use only"; (3) the date after which the preparation is not intended to be used; (4) the storage conditions; (5) the names of any added substances.

Oxytetracycline Hydrochloride



$C_{22}H_{24}N_2O_9, HCl$ Mol. Wt. 496.90

Category : Antibacterial.

Dose : 1 to 2 g daily, in divided doses. By intravenous infusion, in a concentration 0.1 per cent w/v, 1 to 2 g daily.

Description : Pale yellow, crystalline powder; odourless; taste, bitter; hygroscopic.

Solubility : Freely soluble in *water*, the solution becoming cloudy on standing due to liberation of oxytetracycline base; sparingly soluble in *alcohol*; practically insoluble in *chloroform* and in *solvent ether.*

Standards : Oxytetracycline Hydrochloride is (4*S*, 4a*R*, 5*S*, 5a*R*, 6*S*, 12a*S*)-*N*-(2-carbamoyl-1, 4, 4a,5, 5a, 6, 11, 12a-octahydro-3, 5, 6, 10, 12, 12a-hexahydroxy-6-methyl-1, 11-dioxonaphthacen-4-yl) dimethylammonium chloride, a substance produced by the growth of certain strains of *Streptomyces rimosus*, or obtained by any other means. It has a potency equivalent to not less than 835 µg of oxytetracycline, $C_{22}H_{24}N_2O_9$, per mg, calculated with reference to the anhydrous substance.

Identification : (A) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using a coating substance prepared in the following manner: Mix 25 g of *kieselguhr G* with 50 ml of a mixture of 2.5 ml of *glycerin* and 47.5 ml of *0.1M disodium ethylenediaminetetraacetate* previously adjusted to pH 7 with *dilute ammonia*

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

solution. After spreading the plate allow it to stand at room temperature till it is dry (about seventy to ninety minutes). Use as the mobile phase the lower layer formed by shaking 200 ml of a mixture of 2 volumes of *ethyl acetate*, 2 volumes of *chloroform* and 1 volume of *acetone* with 25 ml of *0.1M disodium ethylenediaminetetraacetate* previously adjusted to pH 7 with *dilute ammonia solution*. Apply separately to the plate 1 µl of each of three solutions in *methyl alcohol* containing (1) 0.05 per cent w/v of the substance being examined, (2) 0.05 per cent w/v freshly prepared, of *oxytetracycline hydrochloride R.S.*, (3) 0.05 per cent w/v of *demethylchlortetracycline hydrochloride R.S.*, 0.05 per cent w/v of *oxytetracycline hydrochloride R.S.* and 0.05 per cent w/v of *tetracycline hydrochloride R.S.* After removal of the plate, allow it to dry in air, expose to the vapour of *strong ammonia solution*, and examine under an ultra-violet lamp having a maximum output at about 365 nm. The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2). The separation is not valid unless the chromatogram obtained with solution (3) shows three spots.

(B) Complies with **Identification** tests (B) and (C) described under Oxytetracycline.

(C) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

pH : Between 2.0 and 3.0, determined in a 1.0 per cent w/v solution, Appendix 5.10.

Heavy metals : Not more than 50 parts per million, determined on 0.4 g by Method B, Appendix 3.2.4.

Specific optical rotation : Between −188° and −200°, determined at 20°, on a 1.0 per cent w/v solution in *0.1N hydrochloric acid* after the freshly-prepared solution has been allowed to stand for 60 minutes, Appendix 5.12.

Light absorption : *Extinction* of a 1-cm layer of a 0.002 per cent w/v solution in *buffer solution, pH 2.0*, at the maximum at about 353 nm, about 0.56, Appendix 5.15 A.

Light absorbing impurities : *Extinction* of a 1-cm layer of a 0.2 per cent w/v solution in a mixture of 1 volume of *N hydrochloric acid* and 99 volumes of *methyl alcohol* at 430 nm, not more than 0.50, Appendix 5.15 A. *Extinction* of a 1.0 per cent w/v solution in the same solvent at 490 nm, not more than 0.20, Appendix 5.15 A. Make the measurement within one hour of the preparation of the solutions.

Undue toxicity : Complies with the test described under Bacitracin, the dose being 0.5 ml of a solution containing the equivalent of 1 mg of oxytetracycline dissolved in 0.5 ml of *water for injection*.

Sulphated ash : Not more than 0.5 per cent, Appendix 3.2.7.

Loss on drying : Not more than 2.0 per cent, determined on 1.0 g by drying "in vacuo at 60°" for three hours, Appendix 5.8.

Assay : Use either of the following methods, however, the results obtained from the microbiological assay shall be official.

(1) Carry out the **Assay** (1) described under Oxytetracycline, using *oxytetracycline hydrochloride R.S.* instead of *oxytetracycline R.S.* and express the results in µg of oxytetracycline, $C_{22}H_{24}N_2O_9$ per mg.

(2) Carry out the *microbiological assay of antibiotics, Method A* or *B*, Appendix 4.1, and express the results in µg of oxytetracycline, $C_{22}H_{24}N_2O_9$ per mg.

Oxytetracycline Hydrochloride intended for parenteral administration complies with the following additional requirements:

Histamine-like substances : Complies with the test for *histamine-like substances* described under Oxytetracycline.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using the equivalent of 5 mg of oxytetracycline per kg of the rabbit's weight dissolved in not more than 5 ml of *water for injection*.

Sterility : Complies with the *tests for sterility*, Appendix 4.6.

Storage : Store in tightly-closed, light-resistant containers. If it is intended for parenteral administration, the container should be sterile and sealed so as to exclude micro-organisms.

Labelling : The label on the container states (1) the date after which the contents are not intended to be used; (2) the storage conditions; (3) whether or not the contents are intended for parenteral administration.

Oxytetracycline Capsules

Oxytetracycline Hydrochloride Capsules

Category : Antibiotic.

Dose : Oxytetracycline Hydrochloride, 1 to 3 g daily, in divided doses.

Usual strengths : 250 mg; 500 mg.

Standards : Oxytetracycline Capsules contain not less than 95.0 per cent and not more than 110.0 per cent of the stated amount of Oxytetracycline Hydrochloride.

Identification : (A) The contents of the capsules comply with **Identification** test (A) described under Doxycycline Hydrochloride. Solution (1) is prepared by extracting a quantity of the contents of the capsules equivalent to 10 mg of Oxytetracycline Hydrochloride with 20 ml of

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

methyl alcohol, centrifuging, and using the supernatant liquid; solution (2) is a freshly prepared 0.05 per cent w/v solution of *oxytetracycline R.S.* in *methyl alcohol*.

(B) The contents of the capsules comply with **Identification** tests (A) and (B) described under Oxytetracycline Hydrochloride.

Light absorbing impurities : Dissolve a portion of the mixed contents of 5 capsules as completely as possible in sufficient of a mixture of 1 volume of *N hydrochloric acid* and 99 volumes of *methyl alcohol* to produce two solutions containing the equivalent of (1) 0.20 per cent w/v of Oxytetracycline Hydrochloride and (2) 1.0 per cent w/v of Oxytetracycline Hydrochloride and filter each solution. *Extinction* of a 1-cm layer of the filtrate obtained from solution (1) at 430 nm, not greater than 0.75 and of the filtrate obtained from solution (2) at 490 nm, not greater than 0.40, Appendix 5.15 A.

Loss on drying : Not more than 5.0 per cent, determined on 1.0 g of the mixed contents of the capsules by drying "in vacuo at 60°" for three hours, Appendix 5.8.

Other requirements : Comply with the requirements stated under Capsules.

Assay : Weigh accurately a quantity of the mixed contents of 20 capsules, equivalent to 0.25 g of Oxytetracycline Hydrochloride, add 250.0 ml of *water*, shake, filter and carry out the *microbiological assay of antibiotics, Method A* or *B*, Appendix 4.1, and express the result in mg of Oxytetracycline Hydrochloride per capsule. Each mg of Oxytetracycline is equivalent to 1.078 mg of Oxytetracycline Hydrochloride, $C_{22}H_{24}N_2O_9$, HCl

Storage : Store in tightly-closed, light-resistant containers.

Labelling : The label on the container states (1) the date after which the capsules are not intended to be used; (2) the storage conditions.

Oxytetracycline Eye Ointment

Oxytetracycline Hydrochloride Eye Ointment

Category : Antibacterial.

Usual strength : 10 mg per g.

Standards : Oxytetracycline Eye Ointment contains not less than 90.0 per cent and not more than 115.0 per cent of the stated amount of Oxytetracycline Hydrochloride, $C_{22}H_{24}N_2O_9$, HCl.

Identification : Heat a quantity equivalent to about 20 mg of Oxytetracycline Hydrochloride with 20 ml of *methyl alcohol* for twenty minutes, cool in ice, filter and carefully evaporate on a water-bath to dryness; the residue complies with **Identification** tests (A) and (B) described under Oxytetracycline Hydrochloride.

Water : Not more than 1.0 per cent w/w, Appendix 3.3.25.

Other requirements : Complies with the requirements stated under Eye Ointments.

Assay : Weigh accurately about 1 g and transfer to a separator. Add 25 ml of peroxide-free *solvent ether*, shake well and extract with five successive quantities, each of 20 ml, of *0.1N hydrochloric acid*. Continue the extractions with acid and dilute to 200.0 ml with *0.1N hydrochloric acid*. Dilute a suitable volume with *buffer solution No. 3*, Appendix 4.1, Table 2, to produce a solution containing 1 µg per ml of oxytetracycline hydrochloride. Carry out the *microbiological assay of antibiotics, Method B*, Appendix 4.1, and express the results in mg of Oxytetracycline Hydrochloride per g

Storage : Store in well-closed, containers in a cool place.

Labelling : The label on the container states (1) the date after which the contents are not intended to be used; (2) the storage conditions.

Oxytetracycline Hydrochloride Injection

Category : Antibacterial; antirickettsial.

Dose : By intravenous infusion, the equivalent of 1 to 2 g of oxytetracycline daily in a concentration not exceeding 0.1 per cent w/v in 5 per cent Dextrose Injection or Sodium Chloride Injection.

Usual strengths : The equivalent of 250 mg and 500 mg of tetracycline.

Standards : Oxytetracycline Hydrochloride Injection is a sterile solution of Oxytetracycline in Water for Injection. It is prepared by dissolving the contents of a sealed container in the requisite amount of Water for Injection; the sealed container also contains a suitable buffering agent.

Content of tetracycline : Determine the weight of the contents of each of ten containers as described in the test for **Uniformity of weight** under Injections. Mix the contents of the ten containers and carry out the *microbiological assay of antibiotics, Method A* or *B*, Appendix 4.1. From the result of the assay calculate the proportionate amount of tetracycline in each container. This amount is not less than 90.0 per cent and not more than 115.0 per cent of the amount stated on the label.

Other requirements : Complies with the requirements stated under Injections.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

The contents of the sealed container comply with the following requirements:

Description : Pale yellow, crystalline powder.

Identification : (A) Complies with **Identification** test (A) described under Oxytetracycline Hydrochloride, solution (1) being freshly prepared by shaking a quantity equivalent to 10 mg of oxytetracycline with 20 ml of *methyl alochol*, centrifuging if necessary, and using the clear liquid.

(B) Complies with the **Identification** tests (B) and (C) described under Oxytetracycline Hydrochloride.

Clarity and colour of solution : A 10 per cent w/v solution is clear and yellow.

pH : Between 2.0 and 3.0, determined in a 10 per cent w/v, Appendix 5.10.

Light absorbing impurities : *Extinction* of a 1-cm layer of a solution in a mixture of 1 volume of *N hydrochloric acid* and 99 volumes of *methyl alcohol*, filtered if necessary, containing the equivalent of 0.2 per cent w/v of oxytetracycline at 430 nm, not greater than 0.75, Appendix 5.15 A. *Extinction* of a 1-cm layer of a solution in the same solvent containing the equivalent of 1.0 per cent w/v of oxytetracycline, at 490 nm, not greater than 0.40.

Undue toxicity; Histamine-like substances; Pyrogens; Sterility : Comply with the requirements stated under Oxytetracycline Hydrochloride.

Storage : Store in light-resistant containers. The constituted solution should be used within three days when stored in a cold place.

Labelling : The label on the sealed container states (1) the quantity of Oxytetracycline Hydrochloride contains in it in terms of the equivalent amount of chlortetracycline; (2) the name of the buffering agent; (3) that the contents are to be used for intravenous injection only, in a well-diluted solution; (4) the date after which the contents are not intended to be used; (5) the storage conditions.

Oxytocin Injection

Category : Oxytocic.

Dose : For the induction of labour, by slow intravenous infusion, 1 to 5 Units in 1 litre of 5 per cent Dextrose Injection.

For the stimulation of uterine contractions during labour, by slow intravenous infusion, 1 to 5 Units in 1 litre of 5 per cent Dextrose Injection.

For the control of post-partum haemorrhage, by subcutaneous, intramuscular, or slow intravenous injection, 2 to 5 Units.

Usual strengths : 5 Units per ml; 10 Units per ml.

Description : Clear, colourless liquid.

Standards : Oxytocin Injection is a sterile, aqueous solution containing the oxytocic principle of the posterior lobe of the pituitary body, which may be prepared by a process of fractionation from the glands of oxen or other mammals or by synthesis. It contains not less than 90.0 per cent and not more than 111.0 per cent of the stated potency.

Identification : It gives rise to an appropriate response when used as directed under *biological assay of oxytocin injection*, Appendix 2.12.

pH : Between 2.5 and 4.5, Appendix 5.10.

Vasopressor activity : When assayed by the *biological assay of vasopressin injection*, Appendix 2.13, not greater than 1 Unit (pressor) per 20 Units of oxytocic activity.

Other requirements : Complies with the requirements stated under Injections.

Assay : Carry out the *biological assay of oxytocin injection*, Appendix 2.12. The fiducial limits of error of the estimated potency are not less than 80 per cent and not more than 125 per cent of the stated potency.

Storage : Store at a temperature between 2° and 8°.

Labelling : The label on the container states (1) the potency as the number of Units (oxytocic) per ml; (2) the date after which the contents are not intended to be used; (3) the storage conditions.

Pancreatin

Category : Digestive enzyme.

Dose : 0.5 to 1 g.

Description : White or buff-coloured amorphous powder; odour, meaty and not unpleasant.

Solubility : Soluble in *water* forming a slightly turbid solution; practically insoluble in *alcohol*, and in *solvent ether*.

Standards : Pancreatin is a preparation of mammalian pancreas containing protease, lipase and amylase activity; it may contain Sodium Chloride. It contains not less than the minimum proteolytic

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

activity, amylase activity and lipase activity determined under the conditions of the **Assay**.

Identification : (A) Dissolve 1.5 g in *water*, and divide the resulting solution into three equal portions. Acidify one portion (1) to pH 1.0 by the addition of *N hydrochloric acid*, using *cresol red solution* as indicator, allow to stand for fifteen minutes and then adjust to pH 8.0 by the addition of *N sodium hydroxide*. Adjust the other two portions to pH 8.0 by the addition of *N sodium hydroxide*, using *cresol red solution* as indicator, boil one portion (2) and leave the other (3) untreated. To each portion add a few shreds of *congo red fibrin*, warm to 38° to 40°, and maintain at this temperature for one hour; solution (3) is stained red and solutions (1) and (2) are colourless or not more than slightly pink.

(B) The proteolytic activity is rapidly destroyed in acid solution (distinction from pepsin) and all enzymatic activity is destroyed by boiling an aqueous solution.

(C) Dissolve 1 g in *water*, adjust to pH 8.0, by the addition of *N sodium hydroxide*, using *cresol red solution* as indicator, and divide the solution into two portions; boil one portion to destroy the enzyme. Add 100 mg of *soluble starch* to 100 ml of boiling *water*, boil for two minutes, cool and dilute to 150 ml with *water*. To half the starch solution add the unboiled pancreatin solution, and to the remainder the boiled pancreatin solution and maintain the mixtures at 38° to 40° for five minutes. Transfer 1.0 ml of each mixture to 10 ml of *0.001N iodine*; the liquid containing the unboiled pancreatin solution remains colourless and the liquid containing the boiled pancreatin acquires an intense blue colour.

Fat : Not more than 6.0 per cent, determined by the following method: Extract 1.0 g with *light petroleum (boiling-range 40° to 60°)* for three hours in an apparatus for continuous extraction such as the Soxhlet apparatus, evaporate the extract, and dry the residue at 105° for two hours.

Microbial limits : 1 g is free from *Escherichia coli* and 10 g is free from selmonellae, Appendix 4.5.

Loss on drying : Not more than 5.0 per cent, determined on 1.0 g by drying "in vacuo at 60°" for four hours, Appendix 5.8.

Assay : (1) *For proteolytic activity*—Carry out the *determination of proteolytic activity*, Appendix 2.5, using about 0.5 g, accurately weighed. The difference between the titrations is not less than 4.5 ml.

(2) *For amylase activity*—Not less than 100 units per g determined by the following method: Carry out the *determination of amylase activity*, Appendix 2.4, using as *test solution* 0.1 g or a quantity equivalent to 10 units, accurately weighed and dissolved in sufficient *buffer solution, pH 6.8* to produce 1000.0 ml and beginning at the words "filter if necessary.....".

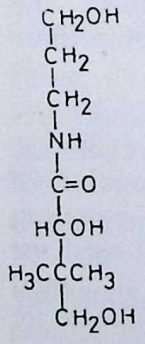
(3) *For lipase activity*—To 95 ml of *water* add 6 5 ml of *triacetin* and 0.2 ml of a 0.1 per cent w/v solution of *bromocresol purple*, neutralise with *0.5N sodium hydroxide* and add sufficient *water* to produce 110 ml. Place 50 ml of this solution in each of two large tubes (3 cm × 20 cm) A and B contained in a thermostat at 30°. Insert in each tube a rubber stopper having two holes, one for the tip of a burette and the other for a short glass tube through which passes a thread operating a glass stirring coil. Stir the contents of the tube until they attain the temperature of the thermostat. Prepare a solution of 0.1 g of the substance being examined in 10 ml of *water*. To tube A add 1 ml of the solution; to tube B add 1 ml of the solution previously boiled. Adjust and maintain the pH of the two tubes between 6.2 and 6.4 by the addition of *0.05N sodium hydroxide* drop by drop, stirring frequently. After thirty minutes, the difference between the amounts of *0.05N sodium hydroxide* added to the two tubes is not less than 1.0 ml.

Storage : Store in tightly-closed, containers, in a cool place.

Labelling : The label on the container states the name of any added substance.

D-Panthenol

Dextro-Pantothenyl Alcohol, Pantothenol



$C_9H_{19}NO_4$ Mol. Wt. 205.25

Category : Vitamin B (enzyme co-factor).

Dose : 0.25 to 0.5 g.

Description : Clear, colourless or slightly yellow, viscous liquid; odourless; taste, bitter; hygroscopic.

Solubility : Miscible with *water* and *alcohol*; sparingly soluble in *chloroform*; slightly soluble in *solvent ether*; insoluble in fats and oils.

Standards : D-Panthenol is (*R*)-2,4-dihydroxy-*N*-(3-hydroxypropyl)-3,3-dimethylbutanamide. It contains not less than 6.60 per cent and not more than 6.95 per cent of nitrogen, N.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Identification : Boil 50 mg in 5 ml of *N sodium hydroxide* for one minute, cool and add *N hydrochloric acid* and two drops of *ferric chloride test-solution*; a strong yellow colour is produced.

Specific optical rotation : Between +28.2° and +30.2°, determined at 20° in a 5.0 per cent w/v solution, Appendix 5.12.

pH : Between 9.2 and 9.6, determined in a 5.0 per cent w/v solution in *carbon dioxide-free water*, Appendix 5.10.

Refractive index : Between 1.490 and 1.498, determined at 20°, Appendix 5.14.

Heavy metals : Not more than 20 parts per million, determined by Method A on 1.0 g dissolved in 25 ml of *water*, Appendix 3.2.4.

Assay : Weigh accurately about 0.5 g and carry out the *determination of nitrogen, Method A*, Appendix 3.3.5. Each ml of *0.1N sulphuric acid* is equivalent to 0.001401 g of N.

Storage : Store in tightly-closed containers.

Papain

Category : Proteolytic enzyme.

Dose : 0.12 to 0.6 g.

Description : White to light brown, amorphous or slightly granular powder; odour, characteristic; taste, faint and characteristic.

Solubility : Sparingly soluble in *water*; practically insoluble in *alcohol*, in *chloroform* and in *solvent ether*.

Standards : Papain is a proteolytic enzyme or a mixture of enzymes obtained from the juice of the unripe fruit of *Carica papaya* Linn. (Fam. Caricaceae). It may contain a suitable harmless diluent such as Lactose.

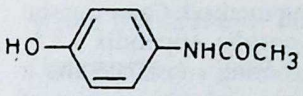
Loss on drying : Not more than 5.0 per cent, determined on 1.0 g by drying "in vacuo at 60°" for four hours, Appendix 5.8.

Proteolytic activity : Weigh accurately about 0.5 g, triturate with 10 ml of *cysteine hydrochloride solution* and dilute to 100.0 ml with *water*. To 30 ml of *water*, in each of two flasks, add 15.0 ml *casein solution* and maintain at 60° by heating on a water-bath. To the first flask add 5.0 ml of the solution containing the sample, and to the second flask add 5.0 ml of the same solution, previously boiled for two minutes and cooled. Maintain the solutions at 60° for thirty minutes, cool rapidly to room temperature and add to each flask 0.75 ml of *phenolphthalein solution* and 10 ml of *formaldehyde solution*, previously neutralised to *phenolphthalein solution*. Titrate both solutions with *0.1N sodium hydroxide* to the same definite pink colour; the difference between the two titrations is not less than 4.5 ml.

Storage : Store in tightly-closed, light-resistant containers, in a cool, dry place.

Paracetamol

Acetaminophen



$C_8H_9NO_2$ Mol. Wt. 151.16

Category : Analgesic and antipyretic.

Dose : 0.5 to 1 g; upto 4 g daily, in divided doses.

Description : White crystals or white crystalline powder, odourless; taste, slightly bitter.

Solubility : Sparingly soluble in *water*, freely soluble in *alcohol*, soluble in *acetone* and in solutions of alkali hydroxides.

Standards : Paracetamol is 4-hydroxyacetanilide. It contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of $C_8H_9NO_2$, calculated with reference to the dried substance.

Identification : (A) Dissolve 0.1 g in 10 ml of *water* and add 0.05 ml of *ferric chloride test-solution*; a violet-blue colour is produced.

(B) Dissolve 50 mg in 100 ml of *methyl alcohol* and mix 1 ml of the solution with 1 ml of *0.1N hydrochloric acid* and sufficient *methyl alcohol* to produce 100 ml; *extinction* of a 1-cm layer of the resulting solution at the maximum at about 249 nm, about 0.44, Appendix 5.15 A.

(C) Boil 0.1 g with 1 ml of *hydrochloric acid* for three minutes, add 10 ml of *water*, and cool; no precipitate is produced. Add 0.05 ml of *0.1N potassium dichromate*; a violet colour slowly develops, which does not become red (distinction from phenacetin).

(D) Dissolve 0.2g in 4 ml of *pyridine*, add 0.5 g of *4-nitrobenzoyl chloride*, boil for two or three minutes, cool, and pour the solution into 40 ml of *water*, stirring continuously. The precipitate, after washing with 30 ml of *water*, 30 ml of a 1 per cent w/v solution of *sodium carbonate*, and 30 ml of *water* and recrystallisation from *alcohol*, melts at about 210°, Appendix 5.11.

Melting range : Between 169° and 172°, Appendix 5.11.

pH : Between 5.3 and 6.5 determined in a saturated solution in *water*, Appendix 5.10.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Heavy Metals : Not more than 10 parts per million, determined by Method B on 2 g, Appendix 3.2.4.

4-Aminophenol : Not more than 0.005 per cent when determined by the following method: Dissolve 0.5 g in sufficient of a mixture of equal volumes of *methyl alcohol* and *water* to produce 10.0 ml, add 0.2 ml of *alkaline sodium nitroprusside solution*, mix and allow to stand for thirty minutes. The solution is not more intensely coloured than 10 ml of a solution prepared at the same time in a similar manner using 0.5 g of *4-aminophenol-free paracetamol* and incorporating 0.5 ml of a 0.005 per cent w/v solution of *4-aminophenol* in the same solvent *mixture*.

4-Chloroacetanilide : Not more than 0.001 per cent when determined by the following method: Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel GF 254* as the coating substance and a mixture of 75 volumes of *hexane* and 25 volumes of *acetone* as the mobile phase, but allowing the solvent front to ascend 14 cm above the line of application, in an unsaturated chamber. Prepare two solutions as follows: For solution (1) transfer 1.0 g to a glass-stoppered, 15-ml centrifuge tube, add 5.0 ml of *solvent ether*, shake mechanically for thirty minutes and centrifuge at 1000 rpm for fifteen minutes or until a clear supernatant is obtained. For solution (2) use a 0.001 per cent w/v solution of *4-chloroacetanilide* in *solvent ether*. Apply separately to the plate 200 µl of solution (1) and 40 µl of solution (2). After removal of the plate, dry it in a current of warm air and examine under an ultra-violet lamp having a maximum output at about 254 nm. Any spot due to 4-chloroacetanilide in the chromatogram obtained with solution (1) is not more intense than the corresponding spot in the chromatogram obtained with solution (2).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in oven at 105°, Appendix 5.8.

Assay : Dissolve 0.3 g in a mixture of 10 ml of *water* and 30 ml of *2N sulphuric acid*. Boil under reflux for one hour, cool, and dilute to 100.0 ml with *water*. To 20 ml of the solution add 40 ml of *water*, 40 g of ice, 15 ml of *2N hydrochloric acid*, 0.1 ml of *ferroin sulphate solution* and titrate with *0.1N ceric ammonium sulphate* until a yellow colour is obtained. Repeat the procedure without the substance being examined. Each ml of *0.1N ceric ammonium sulphate* is equivalent to 0.00756 g of $C_8H_9NO_2$.

Storage : Store in well-closed, light-resistant containers.

Paracetamol Tablets

Category : Analgesic and antipyretic.

Dose : Paracetamol, 0.5 to 1 g; upto 4 g daily, in divided doses.

Usual strengths : 300 mg; 500 mg.

Standards : Paracetamol Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Paracetamol, $C_8H_9NO_2$.

Identification : Extract a quantity of the powdered tablets equivalent to about 0.5 g of Paracetamol with 20 ml of *dry acetone*, filter and evaporate the filtrate to dryness. The residue, after drying at 105°, melts at about 169°, Appendix 5.11, and complies with the **Identification** tests (A) and (C) described under Paracetamol.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.15 g of Paracetamol, add 50 ml of *0.1N sodium hydroxide*, dilute with 100 ml of *water*, shake for fifteen minutes, and add sufficient *water* to produce 200.0 ml. Mix, filter and dilute 10.0 ml of the filtrate to 100.0 ml with *water*. Add 10.0 ml of the resulting solution to 10.0 ml of *0.1N sodium hydroxide*, dilute to 100.0 ml with *water* and mix. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 257 nm, Appendix 5.15 A. Calculate the content of $C_8H_9NO_2$, taking 715 as the value of E(1 per cent, 1-cm) at the maximum at about 257 nm.

Storage : Store in light-resistant containers.

Hard Paraffin

Category : Pharmaceutical aid (stiffening agent).

Description : Colourless or white translucent mass, frequently showing a crystalline structure; odourless even when freshly cut; slightly greasy to the touch. Burns with a luminous flame. When melted, the liquid is free from fluorescence by daylight.

Solubility : Practically insoluble in *water* and in *alcohol*; soluble in *solvent ether* and in *chloroform*.

Standards : Hard Paraffin is a purified mixture of solid hydrocarbons obtained from petroleum or from shale oil.

Congealing range : Between 50° and 65°, Appendix 5.5.

Acidity or Alkalinity : Boil 5 g with 10 ml of *alcohol*, previously neutralised to *litmus solution*; the suspension is neutral to *litmus solution*.

Readily carbonisable substances : Place 5 ml of the melted substance being examined at a temperature just

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

above the melting point, in a dry, heat-resistant, glass-stoppered test-tube 125 mm long and 18 mm in internal diameter, previously rinsed with *chromic acid solution*, then with *water* and dried. Add 5 ml of *sulphuric acid* (containing 94.5 per cent to 95.5 per cent w/w of H_2SO_4), insert the stopper and shake as vigorously as possible, in the longitudinal direction of the tube, for five seconds. Loosen the stopper, immediately place the tube in a bath of boiling water, supporting it so as to prevent contact of the tube with the bottom or side of the bath, and heat for ten minutes. At the end of the second, fourth, sixth, and eighth minute, remove the tube from the bath, and shake as vigorously as possible, in the longitudinal direction of the tube, for five seconds. At the end of ten minutes from the time the tube was placed in the bath, the acid is not more intensely coloured than a mixture of 3 ml of *ferric chloride C.S.*, 1.5 ml of *cobalt chloride C.S.* and 0.5 ml of *copper sulphate C.S.*, overlaid with 5 ml of *liquid paraffin*. If the sulphuric acid remains dispersed in the molten paraffin, the colour of the emulsion is not darker than that of the standard mixture when shaken vigorously.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Storage : Store in well-closed containers.

Light Liquid Paraffin

Light Mineral Oil; Light Liquid Petrolatum

Category : Pharmaceutical aid (vehicle).

Description : Transparent, colourless, oily liquid, free from fluorescence by daylight; almost odourless when cold; tasteless.

Solubility : Practically insoluble in *water*, and in *alcohol*; soluble in *chloroform*, and in *solvent ether*; miscible with fixed and volatile oils.

Standards : Light Liquid Paraffin is a mixture of liquid hydrocarbons, obtained from petroleum. It may contain a suitable stabiliser.

Acidity or Alkalinity : Complies with the test described under Hard Paraffin.

Wt. per ml : Between 0.82 and 0.88 g, Appendix 5.19.

Kinematic viscosity : Not greater than 30 centistokes, determined at 37.8°, Appendix 5.18.

Light absorption : *Extinction* of a 1-cm layer of a 2.0 per cent w/v solution in *iso-octane*, in the range 240 to 280 nm, not greater than 0.1, Appendix 5.15 A.

Readily carbonisable substances : 5 ml complies with the test described under Hard Paraffin.

Solid paraffins : Complies with the test described under Liquid Paraffin.

Sulphur compounds : Mix 4 ml with 2 ml of *ethyl alcohol*, and 2 drops of a clear, saturated solution of *lead monoxide* in *sodium hydroxide solution*, and heat at 70° for ten minutes with frequent shaking; the mixture remains colourless.

Storage : Store in well-closed containers.

Liquid Paraffin

White Mineral Oil; Liquid Petrolatum

Category : Cathartic.

Dose : 8 to 30 ml.

Description : Transparent, colourless, oily liquid, free from fluorescence by daylight; almost odourless; almost tasteless.

Solubility : Practically insoluble in *water*, and in *alcohol*; soluble in *chloroform*, and in *solvent ether*; miscible with fixed and volatile oils.

Standards : Liquid Paraffin is a mixture of liquid hydrocarbons, obtained from petroleum, to which not more than 10 parts per million of tocopherol or of butylated hydroxytoluene may be added.

Light absorption : *Extinction* of a 1-cm layer of a 2.0 per cent w/v solution in *iso-octane*, in the range 240 to 280 nm, not greater than 0.1, Appendix 5.15 A.

Acidity or Alkalinity : Complies with the test described under Hard Paraffin.

Wt. per ml : Between 0.860 g and 0.904 g, Appendix 5.19.

Kinematic viscosity : Not less than 64 centistokes, determined at 37.8°, Appendix 5.18.

Readily carbonisable substances : 5 ml complies with the test described under Hard Paraffin.

Sulphur compounds : Complies with the test described under Light Liquid Paraffin.

Solid paraffins : Place a suitable quantity, previously dried by heating at 100° for two hours and cooled in a desiccator over *sulphuric acid*, in a glass cylindrical vessel having an internal diameter of approximately 25 mm. Close the vessel, and immerse in a mixture of ice and water; after four hours the liquid is sufficiently clear that a black line, 0.5 mm in width, held vertically behind the vessel, is easily seen.

Storage : Store in well-closed, light-resistant containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Yellow Soft Paraffin

Yellow Petroleum Jelly

Category : Pharmaceutical aid (ointment base).

Description : Pale yellow to yellow, translucent soft mass, unctuous to the touch, and retaining these characters on storage and when melted and allowed to cool without stirring; not more than slightly fluorescent by daylight, even when melted; odourless or almost odourless when rubbed on skin.

Solubility : Insoluble in *water* and in *alcohol*; soluble in *chloroform*, in *solvent ether*, and in *light petroleum (boiling range, 40° to 60°)*, the solutions sometime showing a slight opalescence.

Standards : Yellow Soft Paraffin is a semi-solid mixture of hydrocarbons obtained from petroleum.

Melting range : Between 38° and 56°, Appendix 5.11.

Light absorption : *Extinction* of a 1-cm layer of a 0.05 per cent w/v solution in *iso-octane*, at 290 nm, not greater than 0.9, Appendix 5.15 A.

Acidity or Alkalinity : Complies with the test described under Hard Paraffin.

Fixed oils; Fats and rosin; Foreign organic matter : Complies with the tests described under White Soft Paraffin.

Yellow colouring matter : Boil 5 g with 10 ml of *alcohol*; the alcohol is not coloured yellow.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Consistency : Between 100 and 300, determined by the method described under White Soft Paraffin.

Storage : Store in tightly-closed containers.

White Soft Paraffin

White Petroleum Jelly

Category : Pharmaceutical aid (ointment base).

Description : White, translucent, soft mass, unctuous to the touch and retaining these characters on storage and when melted and allowed to cool without stirring; not more than slightly fluorescent by daylight even when melted; odourless when rubbed on the skin.

Solubility : Insoluble in *water* and in *alcohol*; soluble in *chloroform*, in *solvent ether*, and in *light petroleum (boiling range, 40° to 60°)*, the solutions sometimes showing a slight opalescence.

Standards : White Soft Paraffin is a purified mixture of semisolid hydrocarbons obtained from petroleum, and bleached.

Melting range : Between 38° and 56°, Appendix 5.11.

Light absorption : *Extinction* of a 1-cm layer of a 0.05 per cent w/v solution in *iso-octane*, at 290 nm, not greater than 0.5, Appendix 5.15 A.

Acidity or Alkalinity : Complies with the test described under Hard Paraffin.

Fixed oils; Fats and rosin : Digest 10 g with 50 ml of *sodium hydroxide solution* at 100° for thirty minutes, and allow the aqueous layer to separate. On acidifying the aqueous layer with *dilute sulphuric acid* no precipitate or oily matter is produced.

Foreign organic matter : Volatilises when heated, without emitting an acrid odour.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Consistency : Between 100 and 300, determined by the following method:

Apparatus—The apparatus is in agreement, in essential, with Indian Standards IS : 4887–1968 and comprises a penetrometer fitted with a polished cone-shaped metal plunger weighing 150 g having a detachable steel tip of the following dimensions : the tip of the cone has an angle of 30°, the point being truncated to a diameter of 0.38 +0.08 mm, the base of the tip is 8.38 ±0.13 mm in diameter, and the length of the tip is 15 ± 0.25 mm. The remaining portion of the cone has an angle of 90°, is 28 to 29 mm in height, and has a maximum diameter of 65.1 mm at the base. The containers for the test are flat-bottom metal or glass cylinders that are 102 ± 6 mm in diameter and not less than 60 mm in height.

Procedure—Melt a sufficient quantity at a temperature below 85° and pour into one or more of the containers filling to within 6 mm of the rim. Cool to 25 ± 2.5° over a period of not less than 16 hours, protected from drafts. Two hours before the test, place the containers in a water-bath at 25 ± 0.5°. If the room temperature is below 23.5° or above 26.5°, adjust the temperature of the cone to 25 ± 0.5° by placing it in the water-bath.

Without disturbing the surface of the substance under test, place the container on the penetrometer table, and lower the cone until the tip just touches the top surface of the test substance at a spot 25 mm to 38 mm from the edge of the container. Adjust the zero setting and quickly release the plunger, then hold it free for 5 seconds. Secure the plunger, and read the total penetration from the scale. Make three or more trials, each so spaced that there is no overlapping of the areas of penetration. Where the penetration exceeds 20 mm, use a separate container of the test substance for each trial. Read the penetration to the nearest 0.1 mm. Calculate the average of the three or more readings, and conduct further trials to a total of 10 if the

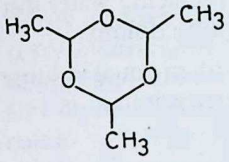
CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

individual results differ from the average by more than ±3 per cent. The final average of the trials is not less than 10.0 mm and not more than 30.0 mm, indicating a consistency value between 100 and 300.

Storage : Store in tightly-closed containers.

Paraldehyde



$C_6H_{12}O_3$ Mol. Wt. 132.16

Category : Hypnotic; sedative; anticonvulsant.

Dose : By intramuscular injection, 2 to 8 ml. By rectal injection, 15 to 30 ml suitably diluted.

Description : Colourless or slightly yellow transparent liquid; odour, strong and characteristic; solidifies at a low temperature to form a crystalline mass.

Solubility : Freely soluble in *water*; miscible with *alcohol (90 per cent)*, with *chloroform*, with *solvent ether*, and with volatile oils.

Standards : Paraldehyde is 2,4,6-trimethyl-1,3,5-trioxane, the trimer of acetaldehyde; it contains a suitable amount of an antioxidant.

Identification : (A) Heat with *dilute sulphuric acid*; acetaldehyde, recognisable by its pungent odour, is produced.

(B) Warm a saturated solution in *water* with *ammoniacal silver nitrate solution* in a test-tube; metallic silver is deposited as a mirror on the sides of the tube.

(C) A 10 per cent v/v solution in *water* is clear but becomes turbid on warming.

Distillation range : Distils completely between 120° and 126°, Appendix 5.3.

Congealing range : Between 10° and 12°, Appendix 5.5.

Refractive index : Between 1.404 and 1.406, Appendix 5.14.

Acidity : Mix 5 ml with 50 ml of freshly boiled and cooled *water*, and titrate with *0.1N sodium hydroxide*, using *phenolphthalein solution* as indicator. Not more than 1.5 ml is required.

Acetaldehyde : Shake 5 ml with 5 ml of *alcohol (60 per cent)*, 5 ml of *hydroxylamine hydrochloride reagent in alcohol (60 per cent)*, and 2 drops of *methyl orange solution*; titrate with *0.5N sodium hydroxide* to the full yellow colour; not more than 0.8 ml is required.

Chloride : To 5 ml of a 1 per cent v/v solution add one drop of *nitric acid* and three drops of *silver nitrate solution*; no opalescence is produced immediately.

Sulphate : To 5 ml of a 1 per cent v/v solution add one drop of *hydrochloric acid* and three drops of *barium chloride solution*; no turbidity is produced.

Peroxidised compounds : Dissolve in a stoppered vessel 5 ml in 75 ml of recently boiled and cooled *water*; add 5 ml of *dilute sulphuric acid* and 10 ml of *potassium iodide solution*. Set aside in the dark for fifteen minutes; titrate with *0.1N sodium thiosulphate* using *starch solution* as indicator; set aside for five minutes and complete the titration. Not more than 2.0 ml of *0.1N sodium thiosulphate* is required.

Paraldehyde intended for parenteral use complies with the following additional requirements:

Sterility : Complies with the *tests for sterility*, Appendix 4.6.

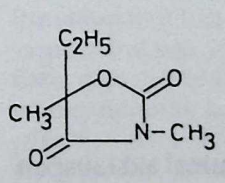
Clarity of solution : Transfer 1 ml to a glass-stoppered cylinder, add 9.5 ml of *isotonic sodium chloride solution* and mix; the solution is clear.

Non-volatile matter : Not more than 0.06 per cent w/v, determined in the following manner: Heat 5 ml in a small dish on a water-bath and dry at 105° for one hour.

Storage : Store in small, well-filled containers, in complete darkness and in a cool place. When solidified, the whole of the contents of the container should be liquefied by warming before use.

Labelling : The label on the container states (1) the nature and the proportion of the antioxidant added; (2) that it may decompose on standing, to form potentially harmful substances.

Paramethadione



$C_7H_{11}NO_3$ Mol. Wt. 157.17

Category : Anticonvulsant.

Dose : 0.9 g daily, in divided doses, increasing to 1.8 g in accordance with the needs of the patient.

Description : Clear, colourless liquid; odour, characteristic and aromatic.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Solubility : Sparingly soluble in *water*; freely soluble in *alcohol*, in *chloroform* and in *solvent ether*.

Standards : Paramethadione is 5-ethyl-3, 5-dimethyloxazolidine-2,4-dione. It contains not less than 98.0 per cent of $C_7H_{11}NO_3$.

Identification : (A) To 5 ml of a 0.5 per cent w/v solution, add *barium hydroxide solution*; a white precipitate is immediately produced.

(B) Heat 0.5 g with 4 ml of *sodium hydroxide solution* on a water-bath for thirty minutes, evaporate to a low bulk; cool in ice, and cautiously add *hydrochloric acid* until the mixture is acid to *congo red paper*. Extract with five quantities, each of 10 ml, of *solvent ether*, remove the ether from the combined extracts and heat on a water-bath for thirty minutes; cool and scratch the container to induce crystallisation. The residue, after recrystallisation from *toluene* melts at about 84°, Appendix 5.11. Heat 50 mg of the crystals with 50 mg of dry *soda lime*; methylamine, recognised by its odour, is evolved and the vapours turn *red litmus paper* blue.

pH : Between 4.0 and 7.5, determined in a 2.5 per cent w/v solution, Appendix 5.10.

Refractive index : Between 1.449 and 1.501, Appendix 5.14.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Assay : Weigh accurately about 0.3 g and gently boil with 150 ml of *water* and 100 ml of *sodium hydroxide solution* for six hours in an ammonia distillation apparatus, collecting any distillate in 40 ml of a 4.0 per cent w/v solution of *boric acid*. Increase the temperature and distil about 200 ml. Cool, add 75 ml of water, distil a further 70 ml into the same receiver, and titrate with *0.1N hydrochloric acid*, using *methyl red solution* as indicator. Repeat the operation without the substance being examined; the difference between the titrations represents the acid required to neutralise the methylamine formed from the paramethadione. Each ml of *0.1N hydrochloric acid* is equivalent to 0.01572 g of $C_7H_{11}NO_3$.

Storage : Store in well-closed containers.

Pectin

Category : Protectant; pharmaceutical aid (suspending agent).

Description : Coarse or fine, yellowish-white powder; almost odourless; taste, mucilaginous.

Solubility : Soluble in *water*, forming a viscous, opalescent, colloidal solution which flows readily; practically insoluble in *alcohol* and in other organic solvents.

Standards : Pectin is a purified carbohydrate product obtained from the dilute acid extract of the inner portion of the rind of citrus fruits or from apple pomace. It consists chiefly of partially methoxylated polygalacturonic acids. It is standardised to yield not less than 7.0 per cent of methoxyl groups ($-OCH_3$) and not less than 78.0 per cent of $C_6H_{10}O_7$ (galacturonic acid), calculated with reference to the ash-free and dried substance.

Identification : (A) Heat 1 g with 9 ml of *water* on a water-bath until a solution is formed, replacing water lost by evaporation; it yields a stiff gel upon cooling.

(B) To a 1 per cent w/v solution, add an equal volume of *alcohol*; a translucent gelatinous precipitate is produced (distinction from most gums).

(C) To 5 ml of a 1 per cent w/v solution, add 1 ml of a 2 per cent w/v solution of *potassium hydroxide* and set aside at room temperature for fifteen minutes; a transparent gel or semi-gel forms (distinction from tragacanth). Acidify the gel with *dilute hydrochloric acid* and shake well; a voluminous, colourless, gelatinous precipitate forms, which upon boiling becomes white and flocculent.

Acidity : An aqueous solution is acid to *blue litmus paper*.

Starch : Boil a 2 per cent w/v solution, cool, and add a few drops of *iodine solution*; no blue colour is produced.

Sugars and organic acids : Place 1 g in a 500-ml flask. Wet it with 3 to 5 ml of *alcohol*. Pour in rapidly 100 ml of *water*; shake well, and allow to stand until solution is complete. To this solution add 100 ml of *alcohol (90 per cent)* containing 0.3 ml of *hydrochloric acid*, mix thoroughly and filter rapidly. Transfer 25 ml of the filtrate to a tared dish, evaporate the liquid on a water-bath and dry the residue "in vacuo at 50°" for two hours. The weight of the residue does not exceed 20 mg.

Arsenic : Not more than 3 parts per million, Appendix 3.2.1.

Lead : Not more than 5 parts per million, determined on 4 g by Method B, Appendix 3.2.6.

Ash : Not more than 4 per cent, Appendix 3.3.22.

Acid-insoluble ash : Not more than 0.4 per cent, Appendix 3.3.22.

Microbial limits : 1 g is free from salmonellae, Appendix 4.5.

Loss on drying : Not more than 10 per cent, determined on 1.0 g by drying in an oven at 105° for two hours, Appendix 5.8.

Assay : *For methoxyl groups*—Weigh accurately 5 g and transfer to a suitable beaker and stir for ten minutes with a mixture of 5 ml of *hydrochloric acid* and 100 ml of *alcohol (60 per cent)*. Transfer to a fritted-glass filter tube and wash with six quantities, each of 15 ml, of the *hydrochlor-*

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

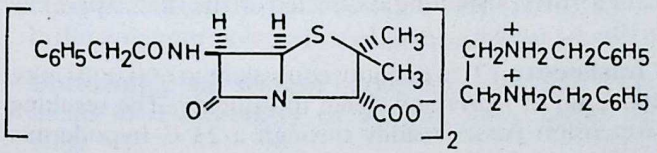
ic acid and *alcohol* mixture, followed by *alcohol (60 per cent)* until the the filtrate is free of chlorides. Wash with 20 ml of *alcohol*, dry in an oven for one hour at 105°, cool and weigh. Transfer exactly one-tenth of the total net weight of the dried sample (representing 500 mg of the original unwashed sample) to a 250-ml Erlenmeyer flask and moisten the sample with 2 ml of *alcohol*. Add 100 ml of recently-boiled and cooled *water* and swirl occasionally until the pectin is completely dissolved. Add five drops of *phenolphthalein solution* and titrate with *0.5N sodium hydroxide* and record the result as the initial titre. Add 20.0 ml of *0.5N sodium hydroxide*, stopper, shake vigorously and set aside for fifteen minutes. Add 20.0 ml of *0.5N hydrochloric acid* and shake until the pink colour disappears. Add three drops of *phenolphthalein solution* and titrate with *0.5N sodium hydroxide* to a faint pink colour which persists after vigorous shaking. Record this value as the saponification titre. Each ml of *0.5N sodium hydroxide* used in the saponification titre is equivalent to 0.01552 g of methoxyl, ($-OCH_3$).

For galacturonic acid—Each ml of *0.5N sodium hydroxide* used in the total titration (the initial titre added to the saponification titre) in the **Assay** for *methoxyl groups* is equivalent to 0.09707 g of $C_6H_{10}O_7$.

Storage : Store in tightly-closed containers.

Benzathine Penicillin

Benzathine Benzylpenicillin; Benzathine Penicillin G



$C_{16}H_{20}N_2,(C_{16}H_{18}N_2O_4S)_2$ Mol. Wt. 909.13

Category : Antibacterial.

Dose : Oral, 0.225 g (300,000 Units) to 0.45 g (600,000 Units) every six hours. By intramuscular injection, 0.225 g (300,000 Units) to 0.75 g (1,000,000 Units)..Prophylactic, by intramuscular injection, 0.9 g (1,200,000 Units) every two or three weeks.

0.9 g is approximately equivalent to 0.72 g of benzylpenicillin (1,200,000 Units of penicillin).

Description : White, crystalline powder; odourless or almost odourless.

Solubility : Very slightly soluble in *water*, freely soluble in *formamide* and in *dimethylformamide*; sparingly soluble in *alcohol*; practically insoluble in *chloroform*, and in *solvent ether*.

Standards : Benzathine Penicillin is *N,N'*-dibenzylethylenediammonium bis [(6*R*)-6-(2-phenylacetamido) penicillanate] containing a variable amount of water of crystallization. It contains not less than 96.0 per cent of total penicillins, calculated as $C_{16}H_{20}N_2$, $(C_{16}H_{18}N_2O_4S)_2$ and not less than 24.0 per cent and not more than 27.0 per cent of $C_{16}H_{20}N_2$, both calculated with reference to the anhydrous substance.

Identification : (A) Shake 0.1 g with 1 ml of *N sodium hydroxide* for two minutes, add 2 ml of *solvent ether*, shake for one minute and allow to separate. Evaporate 1 ml of the ether layer to dryness, dissolve the residue in 2 ml of *glacial acetic acid*, and add 1 ml of *potassium dichromate solution*; a golden yellow precipitate is formed.

(B) Shake 0.1 g with 2 ml of *N sodium hydroxide* for 2 minutes, extract the mixture with two quantities, each of 3 ml, of *solvent ether*, evaporate the combined extracts, and dissolve the residue in 1 ml of *alcohol (50 per cent)*. Add 5 ml of *picric acid solution*, heat at 90° for five minutes, and allow to cool slowly; the precipitate, after recrystallisation from hot *alcohol (25 per cent)* containing a small quantity of *picric acid*, melts at about 214°, Appendix 5.11.

(C) Dilute 0.5 ml of a 1 per cent w/v solution in *formamide* to 5 ml with *water*; the resulting solution is inactivated when treated for two hours with *penicillinase solution*.

pH : Between 5.0 and 7.5, determined in a saturated solution, Appendix 5.10.

Undue toxicity : Complies with the test described under Bacitracin, the dose being 0.5 ml of a suspension containing the equivalent of 0.75 mg of total penicillins in 0.5 ml of *saline solution*.

Water : Between 5.0 and 8.0 per cent w/w, Appendix 3.3.25.

Assay : *For total penicillins*—Weigh accurately about 0.14 g, add a mixture of 40 ml of *methyl alcohol* and 15 ml of *buffer solution, pH 7.2*, dissolve with shaking and dilute to 100.0 ml with *water*. Pipette 10 ml of the resulting solution into a conical flask fitted with a ground glass stopper and add 5.0 ml of *N sodium hydroxide*. Close the flask with a wet stopper, shake and allow to stand for twenty minutes. Add successively 20 ml of *acetate buffer, pH 4.6*, 5.0 ml of *N hydrochloric acid* and 1.4 g of *potassium iodide*. When the potassium iodide has dissolved, add 25.0 ml of *0.02N iodine*. Stopper the flask, shake gently and allow to stand for twenty minutes in the dark. Titrate the excess of iodine with *0.02N sodium thiosulphate* using *starch solution*, added towards the end of the titration, as indicator. To a further 10.0 ml of the initial solution add 20 ml of *acetate buffer, pH 4.6*, 1.4 g of *potassium iodide* and 10 ml of *water*. When the potassium iodide has dissolved, add 25.0 ml of *0.02N iodine* and allow to stand for twenty minutes in the dark.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Titrate the excess of iodine with *0.02N sodium thiosulphate*, using *starch solution*, added towards the end of the titration, as indicator. The difference between the two titrations represents the amount of iodine corresponding to the total penicillins present in the sample.

Calculate the content of total penicillins from the difference obtained by simultaneously carrying out the assay using *benzylpenicillin sodium R.S.* instead of the substance being examined. Each mg of *benzylpenicillin sodium R.S.* is equivalent to 0.001275 g of total penicillins, calculated as $C_{16}H_{20}N_2$, $(C_{16}H_{18}N_2O_4S)_2$.

For $C_{16}H_{20}N_2$—Weigh accurately about 1 g, add 30 ml of *sodium chloride solution* and 10 ml of *sodium hydroxide solution*, shake well, and extract with four quantities, each of 50 ml, of *solvent ether*. Wash the combined extracts with three quantities, each of 10 ml, of *water*, extract the combined washings with 25 ml of *solvent ether*, and add the extract to the main ether solution. Evaporate the ether solution to low bulk, add 2 ml of *ethyl alcohol*, and evaporate to dryness. To the residue, add 50 ml of *glacial acetic acid* and titrate with *0.1N perchloric acid*. Using 1 ml of *1-naptholbenzein solution* as indicator. Repeat the operation without the substance being examined; the difference between the titrations represents the amount of perchloric acid required to neutralise the liberated base. Each ml of *0.1N perchloric acid* is equivalent to 0.01202 g of $C_{16}H_{20}N_2$.

Benzathine Penicillin intended for parenteral administration complies with the following additional requirements.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using a quantity containing the equivalent of 1.5 mg of total penicillins per kg of the rabbit's weight suspended in not more than 5 ml of *water for injection*. A suitable wetting agent may be added to the suspension.

Sterility : Complies with the *test for sterility*, Appendix 4.6.

Storage : Store in well-closed, dry containers in a cool, dry place. If it is intended for parenteral administration, the container should be sterile and sealed so as to exclude micro-organisms.

Labelling : The label on the container states (1) the date after which the contents are not intended to be used; (2) the storage conditions; (3) whether or not the contents are intended for parenteral administration.

Benzathine Penicillin Injection

Category : Antibacterial.

Dose : By intramuscular injection, 1,200,000 to 2,400,000 Units as a single dose; 600,000 to 1,200,000 Units two times a month to three times a week.

Usual strength : 600,000 Units.

Standards : Benzathine Penicillin Injection is a sterile suspension of Benzathine Penicillin in Water for Injection. It is prepared by adding to the contents of a sealed container the requisite amount of Water for Injection; the sealed container may contain a suitable buffering agent and any other suitable pharmaceutical aid.

Content of total penicillins : Determine the weight of the contents of each of ten containers as described in the test for **Uniformity of weight** under Injections. From the result of the **Assay** calculate the proportionate amount of total penicillins in terms of Units of penicillin G in each container. This amount is not less than 95.0 per cent and not more than 110.0 per cent of the amount stated on the label, except that in one container the amount may be not less than 90.0 per cent and not more than 120.0 per cent of the amount stated on the label.

Other requirements : Complies with the requirements stated under Injections.

The contents of the sealed container comply with the following requirements:

Identification : Comply with **Identification** tests (A) and (B) described under Benzathine Penicillin.

pH : Between 5.0 and 7.5, determined in a suspension obtained by reconstituting as directed on the label, Appendix 5.10.

Consistence : To a quantity equivalent to 600,000 Units, add 2 ml of *water* and shake thoroughly. The resulting suspension passes readily through a 23 G hypodermic needle.

Pyrogens : Comply with the *test for pyrogens*, Appendix 2.36, using a quantity containing 2000 Units per kg of the rabbits weight, suspended in not more than 5 ml of *water for injection*.

Undue toxicity : Comply with the test described under Bacitracin, using a quantity containing 1000 Units dissolved in 0.25 ml of *saline solution*.

Water : Between 5.0 per cent and 8.0 per cent w/w, Appendix 3.3.25.

Assay : Carry out the **Assay** *for total penicillins*, described under Benzathine Penicillin, using 0.06 g of the mixed contents of ten containers. Each mg of benzathine penicillin, $C_{16}H_{20}N_2$, $(C_{16}H_{18}N_2O_4S)_2$ is equivalent to 1330 Units of penicillin G.

Storage : Store in single-dose or multiple-dose containers in a cool place. The constituted suspension should be used within seven days or fourteen days,

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

if a buffering agent is present, when stored in a cold place.

Labelling : The label on the sealed container states (1) the quantity of Benzathine Penicillin contains in it in terms of Units; (2) the directions for constituting the suspension; (3) the names of the buffering agent or other pharmaceutical aids; (4) "For intramuscular injection only"; (5) the date after which the contents are not intended to be used; (6) the storage conditions.

Fortified Benzathine Penicillin Injection

Category : Antibacterial.

Dose : The dose is determined by the physician in accordance with the needs of the patient.

Usual strength : Benzathine Penicillin 600,000 Units, Procaine Penicillin 300,000 Units and Benzyl-Penicillin 300,000 Units.

Standards : Fortified Benzathine Penicillin Injection is a sterile suspension of Benzathine Penicillin and Procaine Penicillin in Water for Injection containing Benzylpenicillin in solution. It is prepared by adding the requisite amount of Water for Injection to the contents of a sealed container; the sealed container may contain suitable suspending agents, buffering agents or other pharmaceutical adjuvants.

Uniformity of weight : Complies with the requirements for **Uniformity of weight**, stated under Injections.

Other requirements : Complies with the requirements stated under Injections.

The contents of the sealed container comply with the following requirements:

Identification : (A) Comply with **Identification** tests (A) and (B) described under Procaine Penicillin.

(B) Comply with **Identification** test (A) described under Benzathine Penicillin.

Consistence : To a quantity equivalent to 600,000 Units of Benzathine Penicillin, 300,000 Units of Procaine Penicillin and 300,000 Units of Benzylpenicillin add 2 ml of *water* and shake thoroughly. The resulting suspension passes readily through a 22 G hypodermic needle.

Pyrogens : Comply with the *test for pyrogens*, using a quantity containing 2000 Units of penicillin per kg of rabbit's weight suspended in not more than 5 ml of *water for injection*, Appendix 2.36.

Undue toxicity : Comply with the test for **Undue toxicity**, described under Bacitracin, using a quantity containing 1000 Units of penicillin dissolved in 0.25 ml of *saline solution.*

Water : Not more than 7.5 per cent w/w, Appendix 3.3.25.

Stability : Using an aseptic technique, prepare the injection, as directed on the label, in an individual unopened container immediately before analysis, and determine the concentration of benzylpenicillin by the method described below using an accurately measured volume of the suspension, withdrawn aseptically from the container.

Store the remainder of the injection in the closed container at 4° for seven days and then repeat the determination of benzylpenicillin.

The concentration of benzylpenicillin in the stored injection is not less than 80 per cent of the concentration found in the freshly prepared injection.

Content of benzathine penicillin : Between 90.0 and 125.0 per cent of the stated amount, calculated as Units of penicillin, determined by the following method: Weigh accurately about 1 g, add 30 ml of saturated solution of *sodium chloride* and 10 ml of *sodium hydroxide solution*, shake vigorously, and extract with four successive quantities, each of 50 ml, of *solvent ether*; wash the combined ether extracts with three successive quantities, each of 5 ml, of *water*, extracting each aqueous washing with the same 25 ml of *solvent ether*. Combine the ether extracts, evaporate to a low bulk, add 2 ml of *ethyl alcohol*, evaporate to dryness, dissolve the residue in 50 ml of *glacial acetic acid*, and titrate with *0.1N perchloric acid*, using *1-naphtholbenzein solution* as indicator. Each ml of *0.1N perchloric acid* is equivalent to 0.04545 g of $C_{48}H_{56}N_6O_8S_2$. Calculate the apparent content of Benzathine Penicillin.

Calculate the content of procaine penicillin, as determined by the method given below, in the weight of the sample used in this assay, multiply this content by a factor of 1.544 and deduct the figure from the apparent content of benzathine penicillin; the result is the content of benzathine penicillin. Each mg of benzathine penicillin is equivalent to 1330 Units of penicillin.

Content of procaine penicillin : Between 95.0 per cent and 125.0 per cent of the stated amount, calculated as Units of penicillin, determined by the following method: Weigh accurately about 0.5 g, mix with 100 ml of *water* and dilute to 200.0 ml with *water*, mix well; and filter; dilute 5.0 ml of the filtrate to 250.0 ml with *buffer solution, pH 7.0* and measure the *extinction* of a 1-cm layer at the maximum at about 290 nm, using *buffer solution, pH 7.0* as the blank, Appendix 5.15 A. Calculate the content of procaine penicillin, taking 310 as the value of E(1 per cent, 1-cm) at the maximum at about 290 nm. Each mg of procaine penicillin is equivalent to 1009 Units of penicillin.

Content of benzylpenicillin : Between 90.0 per cent

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

and 130.0 per cent of the stated amount, calculated as Units of penicillin, determined by the following method: Weigh accurately about 4g, add about 4g of *water*, accurately weighed, mix and centrifuge until a clear supernatant liquid is obtained; dilute about 0.6 g of the supernatant liquid, accurately weighed, to 100.0 ml with *water*. Transfer 10.0 ml to a stoppered flask, add 5 ml of *N sodium hydroxide* and allow to stand for twenty minutes; add 20 ml of a freshly prepared buffer solution containing 5.44 per cent w/v of *sodium acetate* and 2.40 per cent w/v of *glacial acetic acid*, 5 ml of *N hydrochloric acid*, and 25.0 ml of *0.02N iodine*, close the flask with a wet stopper, and allow to stand in the dark for twenty minutes. Titrate the excess of iodine with *0.02N sodium thiosulphate*, using *starch solution*, added towards the end of the titration, as indicator.

To a further 10.0 ml of the prepared solution add 20 ml of the buffer solution and 25.0 ml of *0.02N iodine*, allow to stand for twenty minutes in the dark; and titrate with *0.02N sodium thiosulphate*, using *starch solution*, added towards the end of the titration, as indicator. The difference between the two titrations represent the volume of *0.02N iodine* equivalent to the benzylpenicillin present. Calculate the content of benzylpenicillin from the difference obtained by repeating the procedure with *benzylpenicillin sodium R.S.* in place of the substance being examined, and from the declared number of Units per mg of the *benzylpenicillin sodium R.S.*

Storage : Store the sealed container in a cool, dry place. The injection should be used immediately after preparation or within seven days of its preparation provided that it is stored during this period at 2° to 4°.

Labelling : The label on the container states (1) the number of Units of benzathine penicillin, procaine penicillin and benzylpenicillin; (2) the names of the suspending agent, buffering agent or any other pharmaceutical adjuvant added; (3) the words 'for intramuscular injection only'; (4) the date after which the contents are not intended to be used; (5) the storage conditions.

Benzathine Penicillin Tablets

Benzathine Penicillin G Tablets, Benzathine Benzyl-Penicillin Tablets

Category : Antibacterial.

Dose : The equivalent of 300,000 to 600,000 Units, every six hours.

Usual strength : 200,000 Units.

Standards : Benzathine Penicillin Tablets contain a quantity of Benzathine Penicillin equivalent to not less than 90.0 per cent and not more than 110.0 per cent of the stated number of Units of penicillin.

Identification : The powdered tablets comply with **Identification** tests (A) and (B) described under Benzathine Penicillin.

Water : Not more than 8.0 per cent w/w, determined on the powdered tablets, Appendix 3.3.25.

Other requirements : Comply with the requirements stated under Tablets.

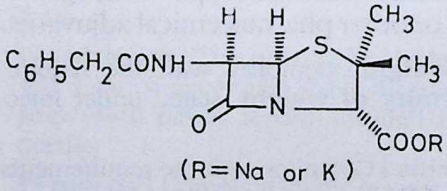
Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 750,000 Units of penicillin and carry out the **Assay** *for total penicillins* described under Benzathine Penicillin. Each mg of benzathine penicillin $C_{16}H_{20}N_2,(C_{16}H_{18}N_2O_4S)_2$ is equivalent to 1330 Units of penicillin.

Storage : Store in well-closed containers in a cool dry place.

Labelling : The label on the container states (1) the strength in terms of Units of penicillin; (2) the date after which the tablets are not intended to be used; (3) the storage conditions.

Benzylpenicillin

Penicillin G



$C_{16}H_{17}N_2NaO_4S$ Mol. Wt. 356.37

$C_{16}H_{17}KN_2O_4S$ Mol. Wt. 372.48

Category : Antibacterial.

Dose : By intramuscular or intravenous injection, 500,000 to 1,000,000 Units daily, in divided doses.

Description : White, fine, crystalline powder; odourless or almost odourless.

Solubility : Very soluble in *water*; soluble in *alcohol*; almost insoluble in fatty oils and in *liquid paraffin*.

Standards : Benzylpenicillin is sodium salt (or the potassium salt) of (6*R*)-6-(2-phenyl-acetamido)-penicillanic acid, produced by the growth of certain

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

strains of *Penicillium notatum* or related organisms or obtained by any other means. It has a potency not less than 1500 Units and not more than 1750 Units per mg (sodium salt) or not less than 1440 Units and not more than 1680 Units per mg (potassium salt).

Identification : (A) It gives the reactions of *penicillins*, and of *sodium* in case of the sodium salt and of *potassium* in the case of the potassium salt, Appendix 3.1.

(B) It is inactivated by *penicillinase solution* when kept in a solution in *water* at pH 6.0 to 7.0 at 57°C.

Specific optical rotation : Not less than +270°, determined in a 2.0 per cent w/v solution in freshly boiled and cooled *water*, Appendix 5.12.

pH : Between 5.5 and 7.5, determined in a 10 per cent w/v solution, Appendix 5.10.

Light absorption : Weigh accurately 0.09 g (sodium salt) or 0.094 g (potassium salt) and dissolve in sufficient *water* to produce 50.0 ml. Measure the *extinction* of a 1-cm layer at 280 nm and at the maximum at about 264 nm, Appendix 5.15 A, scanning at intervals of 0.5 nm, the solution being suitably diluted for the later measurement if necessary. *Extinction* at 280 nm, not more than 0.1; and at the maximum at about 264 nm, between 0.82 and 0.93 calculated on the basis of the undiluted solution (0.18 per cent w/v or 0.188 per cent w/v for the sodium salt or potassium salt, respectively).

Stability : Weigh accurately about 0.1 g in an open vial and heat at 100° for four days. Cool and carry out the **Assay.** Not more than 10 per cent of its content is lost.

Undue toxicity : Complies with the test described under Bacitracin, the dose being 0.5 ml of a solution containing a quantity equivalent to 2000 Units in *water for injection*.

Water : Not more than 1.0 per cent w/w, determined on 1.0 g, Appendix 3.3.25.

Assay : *NOTE—The reagents used must be protected from contamination with penicillinase-producing organisms.*

Weigh accurately about 0.1 g, dissolve in *water* and dilute to 100.0 ml with *water*. Transfer 10.0 ml to a stoppered flask, add 5 ml of *N sodium hydroxide* and allow to stand for 20 minutes. Add 20 ml of a freshly prepared buffer solution containing 5.44 per cent w/v of *sodium acetate*, 2.40 per cent w/v of *glacial acetic acid*, and 5 ml of *N hydrochloric acid* and 25.0 ml of *0.02N iodine*. Close the flask with a wet stopper, and allow to stand for 20 minutes, protected from light. Titrate the excess of iodine with *0.02N sodium thiosulphate*, using *starch solution* added towards the end of the titration, as indicator. To a further 10.0 ml of the initial solution add 20 ml of the buffer solution and 25.0 ml of *0.02N iodine*, allow to stand for twenty minutes, protected from light and titrate with *0.02N sodium thiosulphate*, using *starch solution*, added towards the end of the titration, as indicator. The difference between the two titrations represents the volume of *0.02N iodine* equivalent to the total penicillins present. Simultaneously, carry out the assay using *benzylpenicillin sodium R.S.* to determine the exact equivalent of each ml of *0.02N iodine*. Calculate the potency in Units of penicillin from the declared number of Units of penicillin in *benzylpenicillin sodium R.S.*

Benzylpenicillin intended for parenteral administration complies with the following additional requirements:

Sterility : Complies with the *tests for sterility*, Appendix 4.6.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using 1.5 mg per kg of the rabbit's weight dissolved in not more than 5 ml of *water for injection*.

Storage : Store in well-closed dry containers in a cool, dry place. If it is intended for parenteral administration, store in containers sealed so as to exclude micro-organisms.

Labelling : The label on the container states (1) whether the contents are Benzylpenicillin (sodium salt) or Benzylpenicillin (potassium salt); (2) the total number of Units in the container; (3) the minimum number of Units per mg; (4) whether or not the contents are intended for parenteral administration.

Benzylpenicillin Injection

Penicillin Injection; Penicillin G Injection

Category : Antibacterial.

Dose : By intramuscular or intravenous injection, 500,000 to 1,000,000 Units of benzylpenicillin daily, in divided doses.

Usual strengths : 250,000 Units; 500,000 Units; 1,000,000 Units.

Standards : Benzylpenicillin Injection is a sterile solution of Benzylpenicillin in Water for Injection. It is prepared by dissolving the contents of a sealed container in the requisite amount of Water for Injection, immediately before use; the sealed container may also contain a suitable buffering agent.

Content of benzylpenicillin : Determine the weight of the contents of each of ten containers as described in the test for **Uniformity of weight** under Injections. From the result of the **Assay** calculate the proportionate amount of benzylpenicillin in each container. This amount is not less than 95.0 per cent and not more than 110.0 per cent of the

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

amount stated on the label except that in one container the amount may be not less than 90.0 per cent and not more than 120.0 per cent of the amount stated on the lebel.

Other requirements : Complies with the requirements stated under Injections.

The contents of the sealed container comply with the following requirements:

Description : White or almost white, crystalline powder; practically odourless.

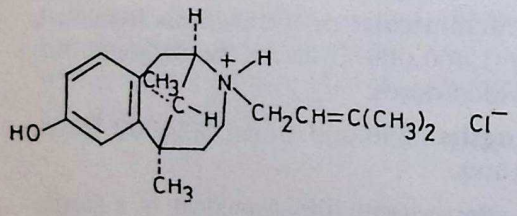
Identification; pH; Water; Pyrogens; Sterility and Undue toxicity : Comply with the requirements stated under Benzylpenicillin.

Assay : Carry out the **Assay** described under Benzylpenicillin, using the mixed contents of ten containers.

Storage : Store in a dry place at a temperature not exceeding 25°. The constituted solution should be used within twenty-four hours when stored at a temperature not exceeding 20° or within seven days (fourteen days, if a buffering agent is present), when stored in a cold place.

Labelling : The label on the sealed container states (1) the quantity of benzylpenicillin in Units, contained in it; (2) whether the contents are Benzylpenicillin (sodium salt) or Benzylpenicillin (potassium salt); (3) the name of any added buffering agent; (4) the date after which the contents are not intended to be used; (5) the storage conditions.

Pentazocine Hydrochloride



$C_{19}H_{27}NO,HCl$ Mol. Wt. 321.89

Category : Analgesic.

Dose : 25 to 100 mg after food.

Description : White or pale cream-coloured crystalline powder; odourless. The material exhibits polymorphism.

Solubility : Freely soluble in *alcohol* and in *chloroform*; soluble in *water*; slightly soluble in *acetone*; practically insoluble in *solvent ether* and in *benzene*.

Standards : Pentazocine Hydrochloride is (2*R**, 6*R**, 11*R**)-1, 2, 3, 4, 5, 6-hexahydro-8-hydroxy-6, 11-dimethyl-3-(3-methylbut-2-enyl)-2,6-methano-3-benzazocinium chloride. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_{19}H_{27}NO,HCl$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *pentazocine hydrochloride R.S.*, Appendix 5.15B.

(B) To 1 mg in a porcelain crucible, add 0.5 ml of a solution of *sulphuric acid* containing 1 per cent w/v of *ammonium molybdate*; an intense blue colour is produced which changes to bluish-green, green and finally, on standing, to yellow.

(C) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

Light absorption : Dissolve 0.10 g in 10 ml of *N hydrochloric acid* and add sufficient *water* to produce 100.0 ml; dilute 10.0 ml to 100.0 ml with *water*; *extinction* of a 1-cm layer of the resulting solution at the maximum at about 278 nm, 0.59 to 0.63, Appendix 5.15A.

pH : Between 4.0 and 6.0, determined in a 1.0 per cent w/v solution, Appendix 5.10.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel HF 254* as the coating substance and a mixture of 94 volumes of *chloroform*, 3 volumes of *methyl alcohol* and 3 volumes of *isopropylamine* as the mobile phase. Apply separately to the plate 10 µl of each of two solutions containing (1) 2 per cent w/v of the substance being examined and (2) 0.02 per cent w/v of *pentazocine hydrochloride R.S.* After removal of the plate, heat at 105° for fifteen minutes, allow to cool, and expose to the vapour of *iodine*. Any spot in the chromatogram obtained with solution (1), other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (2) and not more than two subsidiary spots are present.

Sulphated ash : Not more than 0.2 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying "in vacuo at 100°", Appendix 5.8.

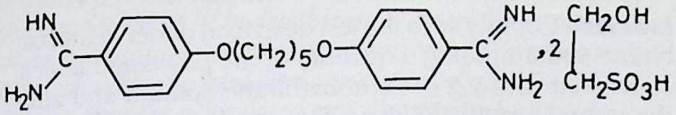
Assay : Weigh accurately about 0.65 g and dissolve in 50 ml of *acetic acid*. Add 10 ml of *mercuric acetate solution*, one or two drops of *crystal-violet solution* and titrate with *0.1N perchloric acid* to a green end point. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.03219g of $C_{19}H_{27}NO,HCl$.

Storage : Store in tightly-closed, light-resistant containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Pentamidine Isethionate



$C_{19}H_{24}N_4O_2,2C_2H_6O_4S$ Mol. Wt. 592.68

Category : Trypenocide.

Dose : By intramuscular injection, 0.3 g.

Description : White or almost white, crystals or powder; odourless; taste, very bitter; hygroscopic.

Solubility : Freely soluble in *water*, slightly soluble in *alcohol*; insoluble in *chloroform* and in *solvent ether*.

Standards : Pentamidine Isethionate is 4,4′-(pentamethylenedioxy) dibenzamidine bis-(2-hydroxyethanesulphonate). It contains not less than 98.5 per cent and not more than the equivalent of 102.5 per cent of $C_{19}H_{24}N_4O_2, 2C_2H_6O_4S$, calculated with reference to the dried substance.

Identification : (A) The light absorption, in the range of 230 to 350 nm, of a 1-cm layer of a 0.001 per cent w/v solution in *0.01N hydrochloric acid* exhibits a maximum only at 262 nm, *extinction* at 262 nm, about 0.46, Appendix 5.15 A.

(B) To 10 ml of a 1 per cent w/v solution, add 1 ml of *dilute sulphuric acid*; a white precipitate is produced.

(C) To 10 ml of a 1 per cent w/v solution, add 0.2 ml of *sodium hydroxide solution*; a white precipitate is produced.

(D) To 10 ml of a 0.05 per cent w/v solution, add 1 ml of a 0.1 per cent w/v solution of *glyoxal sodium bisulphite* and 1 ml of a solution prepared by dissolving 4 g of *boric acid* in a mixture of 27 ml of *N sodium hydroxide* and sufficient *water* to produce 100 ml. Heat on a water-bath for ten minutes; a magenta colour is produced.

Melting range : Between 188° and 192°, Appendix 5.11.

pH : Between 4.5 and 6.5, determined in a 5.0 per cent w/v solution, Appendix 5.10.

Ammonium isethionate : To 1.0 g in a test-tube about 4 cm in diameter add 10 ml of *water* and 20 ml of *N sodium hydroxide*. Immediately attach a bung carrying a splash head and an aspirator tube about 0.5 cm in diameter. Connect the splash head to two test-tubes in series, each containing 20 ml of *0.02N sulphuric acid*. Heat the tube containing the substance being examined in a water-bath at 45° to 50° and, maintaining this temperature, draw a current of air, previously passed through *dilute sulphuric acid*, through the liquids in the series of tubes for three hours at such a rate that the bubbles are just too rapid to count. Titrate the combined solutions from the two absorption tubes with *0.02N sodium hydroxide*, using *methyl red-methylene blue solution* as indicator; not less than 36.5 ml is required.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

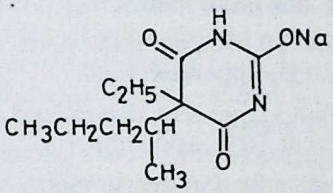
Loss on drying : Not more than 4.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Carry out the *determination of nitrogen, Method A*, Appendix 3.3.5, using about 0.4 g, accurately weighed, and 9 ml of *nitrogen-free sulphuric acid*. Each ml of *0.1N sulphuric acid* is equivalent to 0.01482 g of $C_{19}H_{24}N_4O_2,2C_2H_6O_4S$.

Storage : Store in well-closed containers.

Pentobarbitone Sodium

Soluble Pentobarbitone



$C_{11}H_{17}N_2NaO_3$ Mol. Wt. 248.26

Category : Hypnotic; sedative.

Dose : 0.1 to 0.2 g.

Description : White, crystalline powder or granules; odourless; taste, slightly bitter.

Solubility : Very soluble in *water*, and in *alcohol*; practically insoluble in *solvent ether*.

Standards : Pentobarbitone Sodium is sodium 5-ethyl-5-(1-methylbutyl) barbiturate. It contains not less than 98.5 per cent and not more than the equivalent of 101.5 per cent of $C_{11}H_{17}N_2NaO_3$, calculated with reference to the dried substance.

Identification : (A) Complies with **Identification** test (C) described under Amylobarbitone.

(B) Ignite about 0.2 g; the residue effervesces with acids and gives the reactions of *sodium*, Appendix 3.1.

(C) Melting range of the residue obtained in the **Assay**, 127° to 130°, Appendix 5.11.

Clarity of solution : 1 g dissolves in 10 ml of *carbon dioxide-free water* to give a clear solution.

pH : Between 9.6 and 11.0, determined in a 10 per cent w/v solution, Appendix 5.10.

Free pentobarbitone : Not more than 3.0 per cent, determined by the following method: Weigh accurately

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

about 2 g and dissolve in 75 ml of *dimethyl formamide*; add five drops of a 1 per cent w/v solution of *thymol blue* in *dimethyl formamide* and titrate with *0.1N sodium methoxide* to a blue end-point. Repeat the experiment with the same quantities of the same reagents in the same manner omitting pentobarbitone sodium. Each ml of *0.1N sodium methoxide* is equivalent to 0.02263 g of pentobarbitone.

Isomer : Dissolve 0.3 g in 5 ml of *water* and add 0.3 g of *4-nitrobenzyl bromide* dissolved in 10 ml of *alcohol*. Heat under a reflux condenser for thirty minutes, cool to 25°, and filter. Wash the residue with four quantities, each of 5 ml, of *water*, transfer as completely as possible to a small flask, add 25 ml of *alcohol*, and heat under a reflux condenser for ten minutes; the solid dissolves completely. Cool to 25° and filter; the residue, after drying at 105° for thirty minutes, melts completely between 136° and 148°, Appendix 5.11.

Neutral and basic substances : Carry out the test for **Neutral and basic substances** described under Amylobarbitone, the residue weighs not more than 5 mg.

Heavy metals : Not more than 30 parts per million, determined on 0.67 g by Method B, Appendix 3.2.4.

Loss on drying : Not more than 3.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Carry out the **Assay** described under Amylobarbitone sodium. Each ml of *0.1N alcoholic sodium hydroxide* is equivalent to 0.02483 g of $C_{11}H_{17}N_2NaO_3$.

Storage : Store in well-closed containers.

Pentobarbitone Sodium Tablets

Pentobarbitone Tablets; Pentobarbital Sodium Tablets

Category : Hypnotic; sedative.

Dose : Pantobarbitone Sodium, 0.1 to 0.2 g.

Usual strength : 0.1 g.

Standards : Pentobarbitone Sodium Tablets contain not less than 93.0 per cent and not more than 107.0 per cent of the stated amount of Pentobarbitone Sodium, $C_{11}H_{17}N_2NaO_3$.

Identification : (A) Shake a quantity of the powdered tablets equivalent to 0.1 g of Pentobarbitone Sodium, with 10 ml of a 10 per cent w/v solution of *pyridine* and filter. Add to the filtrate 1 ml of *copper sulphate with pyridine solution* and set aside for ten minutes; a reddish-violet precipitate is produced.

(B) Moisten the powdered tablets with *hydrochloric acid* and introduce on a platinum wire into the flame of a Bunsen burner; a yellow colour is imparted to the flame.

(C) The residue obtained in the **Assay** melts between 127° and 130°, Appendix 5.11.

Isomer : Comply with the test described under Pentobarbitone Sodium, using a quantity of the powdered tablets equivalent to 0.3 g of Pentobarbitone Sodium and after the second heating under a reflux condenser, filtering the hot solution.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Carry out the **Assay** described under Amylobarbitone Sodium Tablets, substituting the words Pentobarbitone Sodium and *pentobarbitone R.S.* with Amylobarbitone Sodium and *amylobarbitone R.S.* respectively.

Storage : Store in well-closed containers.

Pepsin

Category : Proteolytic enzyme.

Dose : 0.3 to 1 g.

Description : White or light buff-coloured, amorphous powder or translucent scales; odour, faint and meaty but not rancid; tests, slightly acid or saline; slightly hygroscopic.

Solubility : Soluble in *water*; yielding an opalescent solution; practically insoluble in *alcohol* and in *solvent ether*.

Standards : Pepsin is a substance containing a proteolytic enzyme obtained from the gastric mucosa of the hog or the cattle. When assayed by the method under **Assay**, it digests not less than 3000 times its weight of coagulated egg albumin. It may contain lactose as a diluent.

Identification : (A) The proteolytic activity of a solution in *water* is destroyed at once by boiling. It is destroyed by warming for ten minutes at 40° at pH 8.0.

(B) Dissolve 1 g in *0.02N hydrochloric acid*; divide the solution into two portions, and boil one to destroy the enzyme; put into each portion a few shreds of *carmine fibrin*, and keep in a thermostat at 38° to 40° for one hour; the unboiled liquid is stained red; the boiled liquid remains almost colourless.

Acidity : Dissolve 0.5 g in 50 ml of *water*, add 0.5 ml of *0.1N sodium hydroxide* and two drops of *phenolphthalein solution*; the solution is red in colour.

Residue on ignition : Not more than 0.5 per cent, determined by igniting to constant weight at red heat.

Loss on drying : Not more than 1.0 per cent, determined by drying 1.0 g in an oven at 80°, Appendix 5.8.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

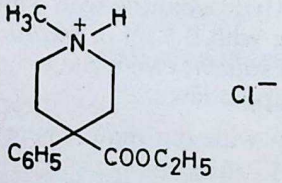
Digitized by Arya Samaj Foundation Chennai and eGangotri

Assay : Weigh accurately 0.25 g and triturate with 1.0 g of *sodium chloride*. Add slowly acidified water prepared by diluting 65 ml of *N hydrochloric acid* to 1000 ml with *water*, continuing the trituration and make the volume to 1000 ml with the acidified water and shake for fifteen minutes. Prepare coagulated egg albumin by boiling fresh hen-eggs in water for fifteen minutes, cooling rapidly to room temperature by immersion in cold water, separating the whites and rubbing through a No. 44 sieve. Reject the first portion that passes through the *sieve* and triturate 15.0 g of freshly prepared coagulated egg albumin with 50 ml of the acidified water ensuring that the particles of egg albumin are thoroughly disintegrated, add a further 50 ml of the acidified water and keep in a water-bath at 50° to 52° for fifteen minutes. Add 20 ml of the prepared pepsin solution and digest at 50° to 52° for four hours; shaking at intervals of fifteen minutes. Centrifuge, and decant off most of the clear supernatant liquid; wash the remainder into a 10 ml graduated cylinder and allow to stand for half an hour. The volume of the undissolved albumin is not greater than 2 ml.

Storage : Store in tightly-closed, containers at a temperature not exceeding 30°C.

Pethidine Hydrochloride

Meperidine Hydrochloride



$C_{15}H_{21}NO_2, HCl$ Mol. Wt. 283.78

Category : Analgesic.

Dose : 25 to 100 mg. By subcutaneous or intramuscular injection, 25 to 100 mg; by intravenous injection, 25 to 50 mg.

Description : Colourless crystals or white crystalline powder; almost odourless; taste, slightly acid and bitter.

Solubility : Freely soluble in *water*; soluble in *alcohol* and in *chloroform*; sparingly soluble in *solvent ether*.

Standards : Pethidine Hydrochloride is 4-ethoxycarbonyl-1-methyl-4-phenylpiperidinium chloride. It contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of $C_{15}H_{21}NO_2, HCl$ calculated with reference to the dried substance.

Identification : (A) To 5 ml of a 1 per cent w/v solution add a few drops of *potassium mercuri-iodide solution*; a cream-coloured precipitate is formed.

(B) Dissolve 5 mg in 0.5 ml of *water* and add 2 drops of *formaldehyde solution*; and 2 ml of *sulphuric acid*; an orange red colour develops.

(C) The light absorption, in the range 230 to 350 nm of a 1-cm layer of a 0.05 per cent w/v solution exhibit maxima, at about 251 nm, 257 nm, and 263 nm, Appendix 5.15 A.

(D) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

Melting range : Between 186° and 190°, Appendix 5.11.

pH : Between 4.0 and 6.0, determined on a 5 per cent w/v solution, Appendix 5.10.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *kieselgubr G* as the coating substance, allowing the solvent front to ascend 12 cm above the line of application. Impregnate the dry plate by placing it in a tank containing a shallow layer of a mixture of 1 volume of *2-phenoxyethanol* and 9 volumes of *acetone*, allowing the impregnating solvent to ascend to the top, removing the plate from the tank, and allowing the acetone to evaporate; use, with the flow of the mobile phase in the direction in which impregnation was carried out, within one hour. Use as the mobile phase the clear supernatant liquid obtained by shaking together 1 volume of *diethylamine*, 100 volumes of *light petroleum (boiling range, 40° to 60°)* and 8 volumes of *2-phenoxyethanol* and allowing to settle. Apply separately to the plate 5 µl of each of the following solutions. For solution (1) dissolve 0.10 g of the substance being examined in 5 ml of *water*, add 0.5 ml of *sodium hydroxide solution* and 2 ml of *solvent ether*, and shake. Allow the layers to separate and use the upper layer. For solution (2) dilute 0.5 ml of solution (1) to 50 ml with *solvent ether*. After removal of the plate, allow the solvent to evaporate at room temperature, return the plate to the tank, close the tank, and again allow the solvent front to ascend 12 cm above the line of application. Remove the plate, allow the solvent to evaporate at room temperature, spray with a 0.2 per cent w/v solution of *2,7-dichlorofluorescein* in *methyl alcohol*, allow to stand for five minutes, and examine under an ultra-violet lamp having a maximum output at about 366 nm. Any spot in the chromatogram obtained with solution (1), other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (2).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.5 g and dissolve in a mixture of 10 ml of *glacial acetic acid* and 12 ml of *mercuric acetate solution*, warming if necessary. Cool

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

and titrate with *0.1N perchloric acid*, using *crystal-violet solution*, as indicator. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02838 g of $C_{15}H_{21}NO_2$,HCl.

Storage : Store in well-closed, light-resistant containers.

Pethidine Injection

Pethidine Hydrochloride Injection; Meperidine Hydrochloride Injection

Category : Analgesic.

Dose : Pethidine Hydrochloride. By subcutaneous or intramuscular injection, 25 to 100 mg; by intravenous injection, 25 to 50 mg.

Usual strength : 50 mg per ml.

Standards : Pethidine Injection is sterile solution of Pethidine Hydrochloride in Water for Injection. It contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of $C_{15}H_{21}NO_2$,HCl.

Identification : (A) On the addition of *picric acid solution*, yellow crystalline needles separate which after washing with water, melt at about 190°, Appendix 5.11.

(B) To 0.5 ml add 2 drops of *formaldehyde solution* and 2 ml of *sulphuric acid*; an orange-red colour develops.

(C) It gives the reactions of *chlorides*, Appendix 3.1.

pH : Between 4.5 and 6.0, Appendix 5.10.

Related substances : Complies with the test described under Pethidine Hydrochloride, using as solution (1) the upper layer obtained by shaking a volume of the Injection equivalent to 0.1 g of Pethidine Hydrochloride diluted if necessary, to 5 ml with *water*, with 0.5 ml *sodium hydroxide solution* and 2 ml of *solvent ether* and allowing the layers to separate.

Other requirements : Complies with the requirements stated under Injections.

Assay : Measure accurately a volume equivalent to about 0.15 g of Pethidine Hydrochloride, transfer to a separator, add 40 ml of *water* and 1 ml of *sodium hydroxide solution*, and extract immediately with 25, 10 and 10 ml of *chloroform*. Wash each extract with the same 15 ml of *water* and filter into a dry flask. Titrate the combined extracts, which should be clear and free from droplets of water, with *0.02N perchloric acid*, using 0.15 ml of *oracet blue B solution* as indicator. Each ml of *0.02N perchloric acid* is equivalent to 0.005676 g of $C_{15}H_{21}NO_2$,HCl.

Storage : Store in single-dose or multiple dose, light-resistant containers.

Pethidine Tablets

Pethidine Hydrochloride Tablets; Meperidine Hydrochloride Tablets

Category : Analgesic.

Dose : Pethidine Hydrochloride, 25 to 100 mg.

Usual strengths : 25 mg; 50 mg.

Standards : Pethidine Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Pethidine Hydrochloride, $C_{15}H_{21}NO_2$, HCl.

Identification : Shake a quantity of the powdered tablets equivalent to 0.2 g of Pethidine Hydrochloride with 20 ml of *water* and filter; to 5 ml of the filtrate add 10 ml of *picric acid solution*; the crystals so obtained, after washing with *water* and drying, melts at about 190°, Appendix 5.11.

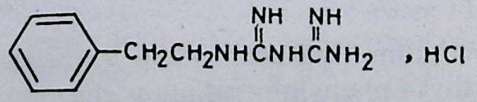
Related substances : Comply with the test described under Pethidine Hydrochloride, using the following as solution (1). Shake a quantity of the powdered tablets equivalent to 0.1 g of Pethidine Hydrochloride with 5 ml of *water*, filter, shake the filtrate with 0.5 ml of *sodium hydroxide solution* and 2 ml of *solvent ether*, allow the layers to separate, and use the upper layer.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Carry out the **Assay** described under Pethidine Injection, using an accurately weighed quantity of the powder equivalent to 0.5 g of Pethidine Hydrochloride.

Storage : Store in well-closed, light-resistant containers.

Phenformin Hydrochloride



$C_{10}H_{15}N_5$, HCl Mol. Wt. 241.74

Category : Oral hypoglycaemic agent.

Dose : 50 to 200 mg daily, in divided doses.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Description : White or almost white, crystalline powder; odourless; taste, bitter.

Solubility : Freely soluble in *water*; soluble in *alcohol*; practically insoluble in *chloroform*, and in *solvent ether*.

Standards : Phenformin Hydrochloride is the hydrochloride of 1-phenethylbiguanide. It contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of $C_{10}H_{15}N_5$, HCl, calculated with reference to the dried substance.

Identification : (A) The light absorption, in the range 220 to 350 nm, of a 1-cm layer of a 0.0005 per cent w/v solution exhibits a maximum only at 234 nm; *extinction* at 234 nm, about 0.3, Appendix 5.15 A.

(B) Dissolve 25 mg in 5 ml of *water*, add 1.5 ml of *sodium hydroxide solution*, 1 ml of *α-naphthol solution*, add dropwise with shaking 0.5 ml of *dilute sodium hypochlorite solution*; a red precipitate is produced which darkens on standing.

(C) Dissolve 10 mg in 10 ml of *water* and add 10 ml of a solution prepared by mixing equal volumes of a 10 per cent w/v solution of *sodium nitroprusside*, a 10 per cent w/v solution of *potassium ferricyanide* and a 10 per cent w/v solution of *sodium hydroxide*. Allow to stand for twenty minutes; a wine-red colour develops within three minutes.

(D) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

Melting range : Between 175° and 179°, Appendix 5.11.

pH : Between 6.0 and 7.0, in a 2.5 per cent w/v solution, Appendix 5.10.

Related biguanides : Prepare three chromatograms by *descending paper chromatography*, Appendix 5.4.2, using a mixture of 6 volumes of *ethyl acetate*, 3 volumes of *alcohol* and 1 volume of *water* to place in the bottom of the tank as the mobile phase. Use three strips of chromatographic paper, 7.5 cm wide. Apply to two of the strips 0.2 ml of a 10 per cent w/v solution of the phenformin hydrochloride in *methyl alcohol*. Place the three strips in the tank and allow elution to proceed until the solvent front has travelled to within 7 cm of the foot of the paper (about five hours). Spray one of the treated strips with a solution prepared as follows: To 1 ml of a 10 per cent w/v solution of *potassium ferricyanide*, add 1 ml of a 10 per cent w/v solution of *sodium nitroprusside* and 1 ml of a 10 per cent w/v solution of *sodium hydroxide*, allow to stand for twenty minutes, add 10 ml of *water* and 12 ml of *acetone*, and mix. Cut from the second treated strip the portion corresponding to the area extending from 3 cm above to 3 cm below any reddish zone appearing at R_f 0.06 to 0.1 on the sprayed strip. Extract the portion, in small pieces, with 20 ml of *methyl alcohol* and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 232 nm, Appendix 5.15 A, using as a blank a solution prepared from the corresponding area of the untreated strip, dissected and extracted in the same manner; the *extinction* is not greater than 0.48.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven to constant weight at 105°, Appendix 5.8.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Assay : Weigh accurately about 0.25 g and dissolve in 10 ml of *glacial acetic acid*, add 10 ml of *mercuric acetate solution* and titrate with *0.1N perchloric acid*, determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.01209 g of $C_{10}H_{15}N_5$, HCl.

Storage : Store in well-closed containers.

Phenformin Tablets

Category : Oral hypoglycaemic agent.

Dose : 50 to 200 mg daily, in divided doses.

Usual strength : 25 mg.

Standards : Phenformin Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Phenformin Hydrochloride, $C_{10}H_{15}N_5$, HCl.

Identification : (A) Shake a quantity of the powdered tablets equivalent to 25 mg of Phenformin Hydrochloride with 200 ml of *water* for 15 minutes, add sufficient *water* to produce 250 ml, filter and dilute 10 ml of the filtrate to 100 ml with *water*; the light absorption of the resulting solution, in the range 220 to 350 nm exhibits a maximum only at 234 nm, Appendix 5.15 A.

(B) Finely powder a quantity of the tablets equivalent to 50 mg of Phenformin Hydrochloride and triturate with 10 ml of *water* and filter; to 5 ml of the filtrate add 1.5 ml of *sodium hydroxide solution*, 1 ml of *α-naphthol solution* and dropwise with shaking, 0.5 ml of *dilute sodium hypochlorite solution*; a red precipitate is produced which darkens on standing.

(C) Shake a quantity of the powdered tablets equivalent to 10 mg of Phenformin Hydrochloride with 10 ml of *water* and filter; the filtrate gives the reactions of *chlorides*, Appendix 3.1.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 40 mg of Phenformin Hydrochloride and shake for 15 minutes with

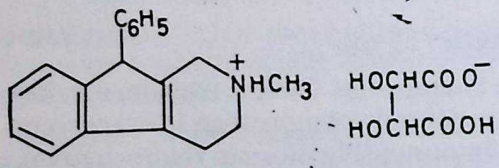
CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

50 ml of *water*, dilute to 100.0 ml with *water* and filter. To 5.0 ml of the filtrate add 10.0 ml of a solution prepared by dissolving 1 g of *sodium nitroprusside* and 1 g of *potassium ferrocyanide* in 50 ml of a 0.5 per cent w/v solution of *sodium hydroxide*, add 5 ml of *strong hydrogen peroxide solution*, swirling gently and diluting to 100 ml with the solution of *sodium hydroxide*. Mix well, and allow to stand for 20 minutes, add sufficient *water* to produce 25.0 ml, and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 520 nm, Appendix 5.15 A, using as the blank a solution prepared by treating 5 ml of *water* in the same manner beginning at the words "add 10.0 ml of a solution.....". Calculate the content of $C_{10}H_{15}N_5$, HCl from the *extinction* obtained by repeating the operation using 5 ml of a 0.04 per cent w/v solution of *phenformin hydrochloride R.S.* and beginning at the words "add 10.0 ml of a solution....." and from the declared content of $C_{10}H_{15}N_5$, HCl in the *phenformin hydrochloride R.S.*

Storage : Store in well-closed containers.

Phenindamine Tartrate



$C_{19}H_{19}N, C_4H_6O_6$ Mol. Wt. 411.45

Category : Antihistaminic.

Dose : 75 to 150 mg daily, in divided doses.

Description : White or creamy-white powder; odour, faint; taste, bitter.

Solubility : Sparingly soluble in *water*; slightly soluble in *alcohol*; practically insoluble in *chloroform* and in *solvent ether*.

Standards : Phenindamine Tartrate is 2,3,4,9-tetrahydro-2-methyl-9-phenyl-1*H*-indeno(2,1-c) pyridinium hydrogen tartrate. It contains not less than 98.5 per cent and not more than the equivalent of 101.0 per cent of $C_{19}H_{19}N, C_4H_6O_6$, calculated with reference to the dried substance.

Identification : (A) Dissolve 25 mg in 5 ml of *sulphuric acid*; an orange-red colour is produced. Dilute carefully the solution with 20 ml of *water*; the colour disappears.

(B) The light-absorption, in the range 230 to 350 nm, of a 1-cm layer of 0.002 per cent w/v solution exhibits a maximum only at 259 nm; *extinction* at 259 nm, about 0.44, Appendix 5.15 A.

(C) Dissolve 0.5 g in 15 ml of hot *water*, add a slight excess of *sodium hydroxide solution*, filter, and neutralise the filtrate to *litmus paper* with *dilute hydrochloric acid*; the solution gives the reactions of *tartrates*, Appendix 3.1.

pH : Between 3.4 and 3.9, determined in a 1.0 per cent w/v solution, Appendix 5.10.

Melting range : Between 160° and 162°, Appendix 5.11, when heated to about 163°, it re-solidifies and at about 168° it melts again with decomposition.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.8 g and dissolve in 20 ml of *glacial acetic acid* and titrate with *0.1 N perchloric acid* using *oracet blue B solution* as indicator. Perform a blank determination and make any necessary correction. Each ml of *0.1 N perchloric acid* is equivalent to 0.04115 g of $C_{19}H_{19}N, C_4H_6O_6$.

Storage : Store in tightly-closed, light-resistant containers.

Phenindamine Tablets

Phenindamine Tartrate Tablets

Category : Antihistaminic.

Dose : Phenindamine Tartrate, 75 to 150 mg daily, in divided doses.

Usual strength : 25 mg.

Standards : Phenindamine Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Phenindamine Tartrate, $C_{19}H_{19}N, C_4H_6O_6$. The tablets may be coated.

Identification : (A) To a portion of the finely powdered tablets equivalent to about 50 mg of Phenindamine Tartrate, add 5 ml of *water* and 3 ml of *dilute ammonia solution* and extract the liberated base with two successive quantities, each of 10 ml, of *solvent ether*. Wash the combined ether extracts with 2 ml of *water* and evaporate to dryness; the residue so obtained complies with **Identification** test (A) described under Phenindamine Tartrate.

(B) Shake a quantity of the powdered tablets equivalent to 20 mg of Phenindamine Tartrate with 100 ml of *water*, dilute 10 ml to 100 ml with *water* and filter. *Extinction* of a 1-cm layer of the filtrate at the maximum at 259 nm about 0.44, Appendix 5.15 A.

Other requirements : Comply with the requirements stated under Tablets.

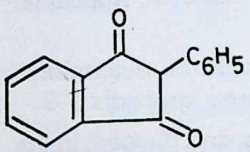
CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Assay : Weigh and digest 20 tablets with 70 ml of *water* and 5 ml of *dilute hydrochloric acid* until completely disintegrated, filter and wash the residue with 20 ml of *water*. Dilute the combined filtrate and washings to 100.0 ml. Measure accurately a quantity of filtrate equivalent to about 0.2 g of Phenindamine Tartrate, add 10 ml of *sodium hydroxide solution*, and extract with 25 ml and then with three quantities, each of 10 ml, of *chloroform*, washing each extract with the same 15 ml *water* and filtering in a dry flask. Titrate the combined extracts (which should be clear and free from droplets of water) with *0.02N perchloric acid* using *oracet blue B solution* as indicator. Perform a blank determination and make any necessary correction. Each ml of *0.02N perchloric acid* is equivalent to 0.008229 g of $C_{19}H_{19}N, C_4H_6O_6$.

Storage : Store in tightly-closed, light-resistant containers.

Phenindione



$C_{15}H_{10}O_2$ Mol. Wt. 222.24

Category : Anticoagulant.

Dose : Initial dose, 200 to 300 mg; subsequent doses, 25 to 100 mg daily, depending on the prothrombin activity of the blood.

Description : White or creamy-white crystals; almost odourless; tasteless.

Solubility : Sparingly soluble in *water*; slightly soluble in *alcohol*, and in *solvent ether*; freely soluble in *chloroform*. Solutions are yellow to red in colour.

Standards : Phenindione is 2-phenylindane-1,3-dione. It contains not less than 98.0 per cent of $C_{15}H_{10}O_2$, calculated with reference to the dried substance.

Identification : (A) Dissolve 0.1 g in 30 ml of *alcohol* with the aid of heat, cool, and add sufficient *alcohol* to produce 50 ml. Dilute 10 ml to 250 ml with *0.1N sodium hydroxide* and dilute 10 ml of the resulting solution to 100 ml with *0.1N sodium hydroxide*. *Extinction* of a 1-cm layer of the resulting solution at 278 nm, about 0.55 and at 330 nm about 0.16, Appendix 5.15 A.

(B) To 1 g add 50 ml of *alcohol* and 0.5 ml of *aniline*, heat gently under a reflux condenser for three hour, cool in ice and filter. The residue after washing with about 2 ml of *alcohol* and recrystallising from *chloroform*, melts at about 225°, Appendix 5.11.

Melting range : Between 148° and 151°, Appendix 5.11.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1 g, by drying in an oven at 105° for three hours, Appendix 5.8.

Assay : Weigh accurately about 0.3 g and dissolve in 50 ml of *alcohol* by warming if necessary. Cool to room temperature, add 10 ml of a 10 per cent v/v solution of *bromine* in *alcohol* and allow to stand for ten minutes, shaking occasionally. Add 1 g of *β-naphthol* and shake until the colour of bromine is discharged. Remove any vapour of bromine in the flask with a current of air, add 50 ml of *water* and 10 ml of *potassium iodide solution*, and titrate the liberated iodine with *0.1N sodium thiosulphate solution* using *starch solution* as indicator. Each ml of *0.1N sodium thiosulphate* is equivalent to 0.01111 g of $C_{15}H_{10}O_2$.

Storage : Store in well-closed containers.

Phenindione Tablets

Category : Anticoagulant.

Dose : Phenindione. Initial dose, 200 to 300 mg; subsequent doses 25 to 100 mg daily, depending on the prothrombin activity of the blood.

Usual strength : 50 mg.

Standards : Phenindione Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Phenindione, $C_{15}H_{10}O_2$.

Identification : (A) Extract a quantity of the powdered tablets equivalent to 0.1 g of Phenindione with *chloroform* and evaporate the extract to dryness. The residue, after recrystallisation from *alcohol*, melts at about 148°, Appendix 5.11, and complies with **Identification** test (A) described under Phenindione.

(B) Shake a quantity of the powdered tablets equivalent to 50 mg of Phenindione with 5 ml of *solvent ether*, filter, and evaporate the filtrate to dryness. Cool the residue and add 1 ml of *sulphuric acid*; a deep blue to violet solution is obtained. On dilution with *water*, the solution becomes colourless and yields a white precipitate.

Other requirements : Comply with the requirements, stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 50 mg of Phenindione and shake with 150 ml of *0.1N sodium hydroxide* for one hour, add sufficient *0.1N sodium hydroxide*

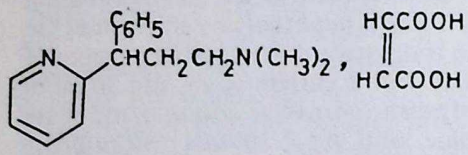
CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

to produce 250.0 ml, filter, and dilute 5.0 ml of the filtrate to 250.0 ml with *0.1N sodium hydroxide*. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 278 nm, Appendix 5.15 A. Calculate the content of $C_{15}H_{10}O_2$, taking 1310 as the value of E(1 per cent, 1-cm) at the maximum at about 278 nm.

Storage : Store in well-closed containers.

Pheniramine Maleate



$C_{16}H_{20}N_2, C_4H_4O_4$ Mol. Wt. 356.42

Category : Antihistaminic.

Dose : 25 to 50 mg daily, in divided doses.

Description : White crystalline powder; odour, faint.

Solubility : Soluble in *water*, and in *alcohol*; slightly soluble in *benzene* and in *solvent ether*.

Standards : Pheniramine Maleate is *N,N*-dimethyl-3-phenyl-3-(2-pyridyl) propylamine hydrogen maleate. It contains not less than 98.5 per cent of $C_{16}H_{20}N_2, C_4H_4O_4$, calculated with reference to the dried substance.

Identification : (A) Dissolve 0.5 g in 5 ml of *water*, add 2 ml of *strong ammonia solution* and extract with three quantities, each of 5 ml, of *chloroform*. Evaporate the aqueous solution to dryness, add 0.2 ml of *dilute sulphuric acid* and 5 ml of *water* and extract with four quantities, each of 25 ml, of *solvent ether* in a current of warm air. The residue melts at about 132°, Appendix 5.11.

(B) Evaporate the chloroform extract obtained in **Identification** test (A) on a water-bath. Add 35 ml of *picric acid solution*, saturated at 65° and maintain at 65° for 20 minutes. Collect the precipitate, wash with a few small portions of *alcohol* and dry at 105° for one hour; the residue melts at about 200°, Appendix 5.11.

(C) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.002 per cent w/v solution in *0.1N hydrochloric acid* exhibits a maximum at 265 nm and an inflection at 262 nm; *extinction* at 265 nm, about 0.42, Appendix 5.15 A.

Melting range : Between 104° and 108°, Appendix 5.11.

pH : Between 4.5 and 5.5, determined in a 1.0 per cent w/v solution, Appendix 5.10.

Heavy metals : Not more than 20 parts per million, determined by Method A on a solution prepared by dissolving 1.0 g in 10 ml of *water*, and adding 2 ml of *acetic acid Sp* and sufficient *water* to produce 25 ml, Appendix 3.2.4.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 5 volumes of *cyclohexane*, 4 volumes of *chloroform* and 1 volume of *diethylamine* as the mobile phase. Apply separately to the plate 10 µl of each of two solutions in *methyl alcohol* containing (1) 2.0 per cent w/v of the substance being examined, (2) 0.0040 per cent w/v of the substance being examined and (3) 0.020 per cent w/v of the substance being examined. After removal of the plate, allow it to dry in air and spray with *dilute potassium iodobismuthate solution*. Any spot in the chromatogram obtained with solution (1), other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (2) except that one spot may be not more intense than the spot in the chromatogram obtained with solution (3).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying at 65° for six hours, Appendix 5.8.

Assay : Weigh accurately about 0.5 g and dissolve in 20 ml of *glacial acetic acid*. Add two drops of *crystal-violet solution* and titrate with *0.1N perchloric acid*. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.01782 g of $C_{16}H_{20}N_2, C_4H_4O_4$.

Storage : Store in tightly-closed, light-resistant containers.

Pheniramine Tablets

Pheniramine Maleate Tablets

Category : Antihistaminic.

Dose : Pheniramine Maleate, 25 to 50 mg daily, in divided doses.

Usual strengths : 12.5 mg; 25 mg; 50 mg.

Standards : Pheniramine Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Pheniramine Maleate, $C_{16}H_{20}N_2, C_4H_4O_4$.

Identification : Boil a quantity of the powdered tablets equivalent to about 0.5g of Pheniramine Maleate with 150 ml of *acetone* under a reflux condenser for about 45 minutes. Filter and evaporate the filtrate to dryness on a

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

water-bath. The residue complies with **Identification** tests (A), (B) and (C) described under Pheniramine Maleate.

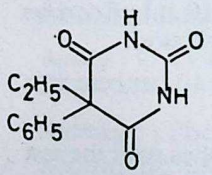
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 250 mg of Pheniramine Maleate and boil under a reflux condenser with 100 ml of *acetone* for about 45 minutes. Cool, decant the supernatant liquid through a sintered-glass funnel. To the residue add 60 ml of *acetone*, reflux for about 45 minutes, transfer the residue and solution to the funnel, and wash the flask and funnel with about 25 ml of *acetone*. Evaporate the filtrate and washings to dryness on a water-bath, add 25 ml of *glacial acetic acid*, agitate and allow to stand for about 15 minutes. Add 2 drops of *crystal-violet solution* and titrate with *0.1N perchloric acid*. Perform a blank titration and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.01782g of $C_{16}H_{20}N_2, C_4H_4O_4$.

Storage : Store in tightly-closed, light-resistant containers.

Phenobarbitone

Phenobarbital



$C_{12}H_{12}N_2O_3$ Mol. Wt. 232.24

Category : Hypnotic; sedative; anti-convulsant.

Dose : Upto 350 mg daily, in divided doses.

Description : White, crystalline powder; odourless; taste, slightly bitter.

Solubility : Very slightly soluble in *water*, soluble in *alcohol* and in *solvent ether*, sparingly soluble in *chloroform*; soluble in aqueous solutions of alkali hydroxides and carbonates.

Standards : Phenobarbitone is 5-ethyl-5-phenylbarbituric acid. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_{12}H_{12}N_2O_3$, calculated with reference to the dried substance.

Identification : (A) Dissolve about 0.1 g in 2 ml of *sulphuric acid*, add a few mg of *sodium nitrite*; a golden yellow colour is produced.

(B) Complies with **Identification** test (C) described under Amylobarbitone.

(C) Dissolve about 20 mg in 5 ml of *alcohol*, add a drop of *cobalt chloride solution*, and a drop of *dilute ammonia solution*; violet colour is produced.

Melting range : Between 174° and 178°, Appendix 5.11.

Acidity : Mix 1.0 g with 50 ml of *water*, boil for two minutes, adjust the volume to 50 ml and filter. To 10 ml of the filtrate add 0.15 ml of *methyl red solution*; not more than 0.1 ml of *0.1N sodium hydroxide* is required to produce the full yellow colour of the indicator.

Clarity and colour of solution : A solution of 0.5 g in 2 ml of *2N sodium hydroxide* and 3 ml of *water* is clear and colourless.

Neutral and basic substances : Carry out the test described under Amylobarbitone; the residue weighs not more than 3 mg.

Phenylbarbituric acid : Boil 1 g for three minutes with 5 ml of *alcohol (90 per cent)* under a reflux condenser; solution is complete.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying at 105° for two hours, Appendix 5.8.

Assay : Weigh accurately about 0.1 g, dissolve in 5 ml of *pyridine*, add 0.25 ml of *thymolphthalein solution*, 10 ml of *silver nitrate-pyridine reagent* and titrate with *0.1N alcoholic sodium hydroxide* until a full blue colour is obtained. Each ml of *0.1N alcoholic sodium hydroxide* is equivalent to 0.011610 g of $C_{12}H_{12}N_2O_3$.

Storage : Store in well-closed containers.

Phenobarbitone Tablets

Phenobarbital Tablets

Category : Hypnotic; sedative; anticonvulsant.

Dose : Phenobarbitone, upto 350 mg daily, in divided doses.

Usual strengths : 15 mg; 30 mg; 60 mg; 100 mg.

Standards : Phenobarbitone Tablets contain not less than 94.0 per cent and not more than 106.0 per cent of the stated amount of Phenobarbitone, $C_{12}H_{12}N_2O_3$.

Identification : (A) Extract a quantity of the powdered tablets equivalent to about 0.5 g of Phenobarbitone with 50 ml of *solvent ether*, filter through *anhydrous sodium sulphate* and evaporate the ether to dryness on a water-bath. The residue complies with **Identification** test (C) described under Amylobarbitone.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

(B) Heat 0.2 g of the residue obtained in **Identification** test (A) on a water-bath with 15 ml of *alcohol (25 per cent)* until dissolved, filter while hot and allow to cool. The crystals after washing with a small quantity of *alcohol (25 per cent)* and drying at 105° melt at about 175°, Appendix 5.11.

Disintegration : Maximum time, 30 minutes, Appendix 5.6.1.

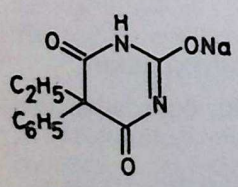
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 50 mg of Phenobarbitone and transfer with the aid of 15 ml of *water* to a separator. Add 5 ml of *dilute hydrochloric acid*, and extract with four quantities, each of 25 ml, of *chloroform*, filtering each extract through chloroform-washed cotton, into a 250-ml volumetric flask. Add *chloroform* to volume, and mix. Transfer 5.0 ml to a beaker, and evaporate the chloroform on a water-bath just to dryness. Transfer the residue to a 100-ml volumetric flask with the aid, first, of 5.0 ml of *alcohol* and then of *buffer solution, pH 9.6* and mix. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 240 nm, Appendix 5.15 A, using *buffer solution, pH 9.6* as the blank. Calculate the content of $C_{12}H_{12}N_2O_3$ from the *extinction* obtained by carrying out the assay simultaneously on 50 mg, accurately weighed, of *phenobarbitone R.S.*, and from the declared content of $C_{12}H_{12}N_2O_3$ in the *phenobarbitone R.S.*

Storage : Store in well-closed, containers.

Phenobarbitone Sodium

Phenobarbital Sodium; Soluble Phenobarbitone



$C_{12}H_{11}N_2NaO_3$ Mol. Wt. 254.22

Category : Hypnotic; sedative.

Dose : Upto 350 mg daily, in divided doses.

By intravenous, intramuscular or subcutaneous injection, 50 to 200 mg.

Description : White powder or crystalline granules or flaky crystals; odourless; taste, bitter. Hygroscopic.

Solubility : Very soluble in *water*; soluble in *alcohol*; practically insoluble in *chloroform* and in *solvent ether*.

Standards : Phenobarbitone Sodium is sodium 5-ethyl-5-phenylbarbiturate. It contains not less than 98.0 per cent of $C_{12}H_{11}N_2NaO_3$, calculated with reference to the dried substance.

Identification : (A) Dissolve 0.5 g in 15 ml of *water*, add 5 ml of *dilute hydrochloric acid* and extract with 50 ml of *solvent ether*. Evaporate the ethereal extract to low bulk, add 2 ml of *ethyl alcohol*, evaporate to dryness and dry the residue at 105°. Heat 0.2 g of the residue with 15 ml of *alcohol (25 per cent)* until dissolved, allow to cool, filter through a sintered-glass crucible, wash with a small quantity of *alcohol (25 per cent)* and dry at 105° for one hour. The crystals comply with the following tests: (a) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *phenobarbitone R.S.*, Appendix 5.15B; (b) They melt at about 175°, Appendix 5.11.

(B) A solution of 0.25 g in 5 ml of *water* is alkaline to *litmus solution*; on acidification with *dilute hydrochloric acid* it gives a white precipitate.

(C) Ignite about 0.1 g; the residue gives the reactions of *sodium*, Appendix 3.1.

(D) 1 g completely dissolves in 20 ml of *alcohol (90 per cent)* (distinction from barbitone-sodium).

Clarity of solution : 1 g dissolves in 10 ml of *carbon dioxide-free water* to produce a clear solution.

pH : Not more than 11, determined in a 10 per cent w/v solution, Appendix 5.10.

Neutral and basic substances : Complies with the test described under Amylobarbitone.

Heavy metals : Not more than 30 parts per million, determined by Method A on the solution obtained in the following manner: Dissolve 2 g in 52 ml of *water*, add with vigorous stirring 8 ml of *N hydrochloric acid*, filter and reject the first 5 ml of the filtrate; dilute 20 ml of the subsequent filtrate to 25 ml with *water*, Appendix 3.2.4.

Loss on drying : Not more than 7.0 per cent, determined on 1.0 g by drying in an oven at 130°, Appendix 5.8.

Assay : Weigh accurately about 0.5 g and dissolve in 30 ml of *glacial acetic acid*, add 10 ml of *mercuric acetate solution* and a few drops of *1-naphtholbenzein solution*. Titrate with *0.1N perchloric acid* to a green end-point. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02542 g of $C_{12}H_{11}N_2NaO_3$.

Storage : Store in well-closed containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Phenobarbitone Sodium Injection

Soluble Phenobarbitone Injection; Soluble Phenobarbital Injection

Category : Hypnotic; sedative.

Dose : Phenobarbitone Sodium, by intravenous, intramuscular or subcutaneous injection, 50 to 200 mg.

Standards : Phenobarbitone Sodium Injection is a sterile solution of Phenobarbitone Sodium in Water for Injection free from carbon dioxide. It is prepared immediately before use by dissolving the contents of a sealed container in the requisite amount of water free from carbon dioxide, under aseptic conditions. The sealed container contains not less than 98.0 per cent of Phenobarbitone Sodium, $C_{12}H_{11}N_2NaO_3$, calculated with reference to the dried substance.

Uniformity of weight : Complies with the requirements for **Uniformity of weight**, test (1), stated under Injections.

Other requirements : Comply with the requirements stated under Injections.

The contents of the sealed container comply with the following requirements:

Identification; Clarity of solution; pH; Neutral and basic substances; Heavy metals and Loss on drying : Comply with the requirements described under Phenobarbitone Sodium.

Assay : Carry out the **Assay** described under Phenobarbitone Sodium.

Storage : Phenobarbitone Sodium Injection should be used immediately after preparation. It deteriorates on storage.

Phenobarbitone Sodium Tablets

Soluble Phenobarbitone Tablets; Soluble Phenobarbital Tablets

Category : Hypnotic; sedative.

Dose : Phenobarbitone Sodium, upto 350 mg daily, in divided doses.

Usual strength : 30 mg.

Standards : Phenobarbitone Sodium Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Phenobarbitone Sodium, $C_{12}H_{11}N_2NaO_3$.

Identification : (A) Triturate a quantity of the powdered tablets equivalent to about 0.5 g of Phenobarbitone Sodium with 10 ml of *water*; add 5 ml of *dilute hydrochloric acid* and carry out **Identification** test (A) described under Phenobarbitone Sodium. The crystals obtained comply with the test for *infra-red absorption spectrum*, Appendix 5.15B, and melt at about 175°, Appendix 5.11.

(B) Triturate a quantity of the powdered tablets equivalent to 0.2 g of Phenobarbitone Sodium with 5 ml of *water* and filter; the filtrate is alkaline to *litmus solution* and yields a white precipitate on the addition of *dilute hydrochloric acid.*

(C) The powdered tablets give the reactions of *sodium*, Appendix 3.1.

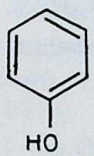
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.3 g of Phenobarbitone Sodium and carry out the **Assay** described under Phenobarbitone Sodium.

Storage : Store in well-closed containers.

Phenol

Carbolic Acid



C_6H_6O Mol. Wt. 94.11

Category : Antiseptic; topical, antipruritic; pharmaceutical aid (preservative).

Description : Colourless or pinkish, needle-shaped, deliquescent crystals or crystalline masses; odour, characteristic and not tarry; caustic.

Solubility : Soluble in *water*; freely soluble in *alcohol*, in *solvent ether*, in *chloroform*, in *glycerin* and in fixed and volatile oils.

Standards : Phenol contains not less than 98.0 per cent and not more than the equivalent of 100.5 per cent of C_6H_6O, calculated with reference to the anhydrous substance.

Identification : (A) To 10 ml of a solution (1 in 100) add one drop of *ferric chloride test-solution*; a violet colour is produced.

(B) A 1 per cent w/v solution gives with *bromine solution* a white precipitate, which on the continued addition

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

of the reagent, at first dissolves and then becomes permanent.

Congealing temperature : Not below 39.5°, Appendix 5.5.

Clarity and acidity of solution : A solution of 1 part in 15 parts of *water* is clear; mix 5 ml of the solution with 5 ml of *water* and one drop of *methyl orange solution*; a yellow but no orange or red colour is produced.

Non-volatile matter : Not more than 0.05 per cent, when volatilised on a water-bath and dried to constant weight at 105°

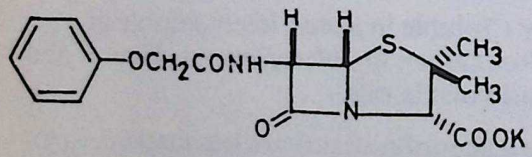
Water : Not more than 0.5 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately about 0.5 g and dissolve in sufficient *water* to produce 500.0 ml. Mix 25.0 ml of this solution with 25.0 ml of *0.1N potassium bromate* in a 250.0 ml glass-stoppered flask, and add 1 g of powdered *potassium bromide* and 10 ml of *dilute hydrochloric acid*. Insert the stopper, previously moistened with a few drops of a 10.0 per cent w/v solution of *potassium iodide*, and set aside in the dark for twenty minutes with frequent shaking. Add 10 ml of a 10.0 per cent w/v solution of *potassium iodide*, shake and allow to stand in the dark for a further five minutes. Wash the stopper and neck of the flask with *water*, add 10 ml of *chloroform* and titrate the liberated iodine with *0.1N sodium thiosulphate* using *starch solution* as indicator. Perform a blank determination and make any necessary correction. Each ml of *0.1N potassium bromate* is equivalent to 0.001569 g of C_6H_6O.

Storage : Store in well-closed, light-resistant containers, in a cool place.

Phenoxymethylpenicillin Potassium

Penicillin V Potassium



$C_{16}H_{17}KN_2O_5S$ Mol.Wt. 388.48

Category : Antibacterial.

Dose : The equivalent of 0.5 to 1.5 g of phenoxymethylpenicillin daily, in divided doses.

Description : White, fine crystalline powder; odourless or with a slight characteristic odour; taste, slightly bitter.

Solubility : Freely soluble in *water*; slightly soluble in *alcohol*; insoluble in *solvent ether*.

Standards : Phenoxymethylpenicillin Potassium is potassium (6*R*)-6-(2-phenoxyacetamido)penicillanate. It contains not less than 87.0 per cent of total penicillins, calculated as $C_{16}H_{18}N_2O_5S$ with reference to the dried substance.

Identification : (A) It gives the reactions of *penicillins*, Appendix 3.1.

(B) Dissolve 10 mg in 10 ml of *water* and add 0.5 ml of *neutral red solution*. Add sufficient *0.01N sodium hydroxide* to give a permanent orange colour. Add 1.0 ml of *penicillinase solution*; the colour changes to red.

(C) Ignite; the residue gives the reactions of *potassium*, Appendix 3.1.

pH : Between 5.0 and 7.5 determined in a 0.5 per cent w/v solution, Appendix 5.10.

Light absorption : Dissolve 0.1 g in sufficient *0.1N sodium hydroxide* to produce 100 ml; *extinction* of the resulting solution at the maximum at about 306 nm, not greater than 0.325, Appendix 5.15 A. Dilute 20 ml to 100 ml with *0.1N sodium hydroxide*; *extinction* of the resulting solution at the maximum at about 274 nm, not less than 0.5.

Phenoxyacetic acid : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 80 volumes of *chloroform*, 10 volumes of *methyl alcohol* and 15 volumes of *anhydrous formic acid* as the mobile phase. Apply separately to the plate 5 µl of each of the following solutions: For solution (1) dissolve 0.4 g in sufficient *buffer solution, pH 6.0* to produce 10 ml and for solution (2) dissolve 20 mg of *phenoxyacetic acid* in sufficient *buffer solution, pH 6.0* to produce 100 ml. After removal of the plate, allow it to dry in air, spray with a 0.15 per cent w/v solution of *potassium permanganate* in a 5 per cent w/v solution of *sulphuric acid* and dry at 100° for ten minutes. The spot in the chromatogram obtained with solution (2) is more intense than any corresponding spot in the chromatogram obtained with solution (1).

Undue toxicity : Complies with the test described under Bacitracin, using 0.66 mg dissolved in 0.5 ml of *saline solution*.

Loss on drying : Not more than 1.5 per cent, determined on 1.0 g by drying in an oven at 105° Appendix 5.8.

Assay : Carry out the **Assay** described under Benzylpenicillin, using *phenoxymethylpenicillin R.S.* in place of *benzylpenicillin sodium R.S.* Each mg of *phenoxymethyl penicillin potassium R.S.* is equivalent to 0.9019 mg of total penicillins, calculated as $C_{16}H_{18}N_2O_5S$.

Storage : Store in tightly-closed containers.

Labelling : The label on the container states (1) the

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

date after which the contents are not intended to be used; (2) the storage conditions.

Phenoxymethylpenicillin Potassium Tablets

Category : Antibacterial.

Dose : The equivalent of 0.5 to 1.5 g of phenoxymethylpenicillin daily, in divided doses.

Usual strengths : The equivalent of 62.5 mg, 125 mg, 250 mg and 500 mg of phenoxymethylpenicillin.

Standards : Phenoxymethylpenicillin Potassium Tablets contain a quantity of Phenoxymethylpenicillin Potassium equivalent to not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of phenoxymethylpenicillin, $C_{16}H_{18}N_2O_5S$. The tablets may be coated.

Identification : (A) Disperse a quantity of the powdered tablets equivalent to 0.1 g of phenoxymethylpenicillin in sufficient *water* to produce 500 ml and filter. A 1-cm layer of the filtrate so obtained exhibits light absorption with maxima at 268 nm and 274 nm and a minimum at 272 nm; *extinction* at 268 nm, about 0.70, Appendix 5.15 A.

(B) To 5 ml of a saturated solution add three drops of *dilute hydrochloric acid*, mix, cool in ice, add one drop of a 10 per cent w/v solution of *sodium nitrite*, then add a solution of 50 mg of *β-naphthol* in a mixture of 2 ml of *N sodium hydroxide* and 3 ml of *water*; no scarlet-red precipitate is formed (absence of Procaine Penicillin G).

(C) Ignite 0.5 g of the powdered tablets, add 5 ml of *2N hydrochloric acid*, boil, cool and filter; the filtrate gives the reactions of *potassium*, Appendix 3.1.

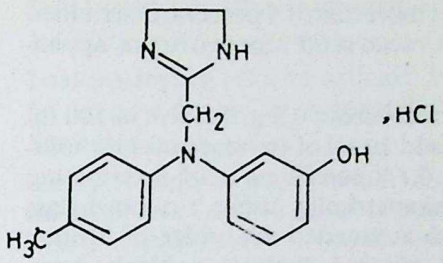
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.1 g of phenoxymethylpenicillin and shake with 80 ml of *water* for five minutes, dilute to 100.0 ml with *water* and filter. Using the filtrate so obtained, carry out the **Assay** for total penicillins described under Benzylpenicillin, beginning at the words "Transfer 10.0 ml....".

Storage : Store in tightly-closed containers.

Labelling : The label on the container states (1) the strength in terms of the equivalent amount of phenoxymethylpenicillin; (2) the date after which the tablets are not intended to be used; (3) the storage conditions.

Phentolamine Hydrochloride



$C_{17}H_{19}N_3O$, HCl Mol.Wt. 317.82

Category : Anti-adrenergic.

Dose : 50 mg, four to six times a day.

Description : White or almost white, crystalline powder; odourless; taste, bitter.

Solubility : Sparingly soluble in *water*; slightly soluble in *alcohol*; very slightly soluble in *chloroform* and in *solvent ether*.

Standards : Phentolamine Hydrochloride is the hydrochloride of 3-[*N*-(2-imidazolin-2-ylmethyl)-*p*-toluidino]phenol. It contains not less than 98.0 per cent of $C_{17}H_{19}N_3O$, HCl, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the wavelengths as, and have similar relative intensities to, those in the spectrum of *phentolamine hydrochloride R.S.*, Appendix 5.15 B.

(B) Dissolve 20 mg in 10 ml of *water* and add a few ml of *picric acid solution*, a yellow precipitate is produced.

(C) Dissolve 20 mg in 10 ml of water and add a few ml of *ammonium reineckate solution*; a pink precipitate is produced.

(D) A solution (1 in 500) gives the reactions of *chlorides*, Appendix 3.1.

Melting range : Between 238° and 242°, Appendix 5.11.

Foreign substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 15 volumes of *acetone*, 85 volumes of *ethyl methyl ketone* and 5 volumes of *strong ammonia solution* as the mobile phase. Apply separately to the plate 10 µl of each of two solutions in *alcohol* containing (1) 2.0 per cent w/v of the substance being examined and (2) 0.01 per cent w/v of the substance being examined. After removal of the plate allow it to dry in air, and spray with *dilute potassium iodobismuthate solution*. Any spot in the chromatogram obtained with solution (1) other than the principal spot is not more intense than the spots in the chromatogram obtained with solution (2).

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

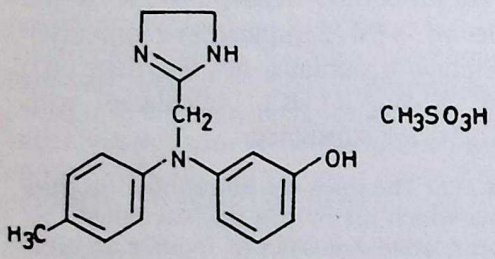
Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying "in vacuo at 60°" for two hours, Appendix 5.8.

Assay : Weigh accurately about 0.5 g, dissolve in 100 ml of *methoxyethanol*, add 10 ml of *mercuric acetate solution* and titrate with *0.1N perchloric acid*, determining the end-point potentiometrically, using a calomel-glass electrode system with a saturated salt bridge of *lithium chloride* in *methyl alcohol*. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.03178 g of $C_{17}H_{19}N_3O$, HCl.

Storage : Store in tightly-closed, light-resistant containers.

Phentolamine Mesylate



$C_{17}H_{19}N_3O, CH_3SO_3H$ Mol. Wt. 377.46

Category : Anti-adrenergic.

Dose : By intravenous injection, 5 to 10 mg.

Description : White, crystalline powder; odourless; taste bitter. Slightly hygroscopic.

Solubility : Freely soluble in *water* and in *alcohol*; slightly soluble in *chloroform*.

Standards : Phentolamine Mesylate is 3-[*N*-(2-imidazolin-2-ylmethyl)-*p*-toluidino]-phenol methanesulphonate. It contains not less than 99.0 per cent of $C_{17}H_{19}N_3O,CH_3SO_3H$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *phentolamine mesylate R.S.*, Appendix 5.15 B.

(B) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.002 per cent w/v solution exhibits a maximum only at 278 nm; *extinction* at 278 nm, about 0.5, Appendix 5.15 A.

(C) Dissolve 0.5 g in 5 ml of *alcohol* and 5 ml of *0.1N hydrochloric acid* and add 2 ml of a 0.5 per cent w/v solution of *ammonium vanadate*; a light green precipitate is produced.

(D) Mix 50 mg with 0.2 g of powdered *sodium hydroxide*, heat to fusion and continue the heating for a few seconds longer. Cool, add 0.5 ml of *water* and a slight excess of *dilute hydrochloric acid*, and warm. Sulphur dioxide is evolved which turns moistened *starch-iodate paper* blue.

Melting range : Between 175° and 181°, Appendix 5.11.

Acidity or Alkalinity : Dissolve 0.1 g in 10 ml of *carbon dioxide-free water*. The solution is not alkaline to *methyl red solution* and requires not more than 0.05 ml of *0.1N sodium hydroxide* to make it alkaline.

Foreign substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 15 volumes of *acetone*, 85 volumes of *ethyl methyl ketone*, and 5 volumes of *strong ammonia solution* as the mobile phase. Apply separately to the plate 10 µl of each of two solutions in *alcohol* containing (1) 2.0 per cent w/v of the substance being examined and (2) 0.01 per cent w/v of the substance being examined. After removal of the plate, allow it to dry in air, and spray with *dilute potassium iodobismuthate solution*. Any spot in the chromatogram obtained with solution (1), other than the principal spot is not more intense than the spot in the chromatogram obtained with solution (2)

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

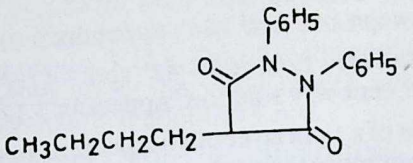
Assay : Weigh accurately about 0.3 g and dissolve in 100 ml of *isopropyl alcohol*. Titrate in an atmosphere of *nitrogen* with *0.1N tetrabutylammonium hydroxide* in *isopropyl alcohol*, determining the end-point potentiometrically, using a glass electrode and a calomel electrode containing a saturated solution of *tetramethylammonium chloride* in *isopropyl alcohol*. Perform a blank determination and make any necessary correction. Each ml of *0.1N tetrabutylammonium hydroxide* is equivalent to 0.03775 g of $C_{17}H_{19}N_3O, CH_3SO_3H$.

Storage : Store in tightly-closed, light-resistant containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Phenylbutazone



$C_{19}H_{20}N_2O_2$ Mol. Wt. 308.38

Category : Anti-inflammatory; analgesic.

Dose : 100 to 600 mg daily, in divided doses.

Description : White or almost white, crystalline powder; odourless.

Solubility : Very slightly soluble in *water*; freely soluble in *acetone*, and in *solvent ether;* soluble in *alcohol.*

Standards : Phenylbutazone is 4-butyl-1, 2-diphenyl pyrazolidine-3, 5-dione. It contains not less than 98.0 per cent and not more than the equivalent of 100.5 per cent of $C_{19}H_{20}N_2O_2$, calculated with reference to the dried substance.

Identification : (A) The light absorption, in the range 240 to 350 nm of a 1-cm layer of a 0.0005 per cent w/v solution in *0.01N sodium hydroxide* exhibits a maximum at about 264 nm; *extinction* at 264 nm, about 0.33, Appendix 5.15 A.

(B) To 0.1 g add 1 ml of *glacial acetic acid* and 2 ml of *hydrochloric acid* and heat on a water-bath for thirty minutes. Cool, add 10 ml of *water* and filter. To the filtrate add 3 ml of *0.1M sodium nitrite*; a yellow colour is produced. Add 1 ml of the solution to 5 ml of *β-naphthol solution*; a brownish-red precipitate is formed which dissolves on the addition of *alcohol*, yielding a red solution.

Melting range : Between 104° and 107°, Appendix 5.11.

Clarity and colour of solution : Dissolve 1.0 g by shaking with 20.0 ml of *2N sodium hydroxide* and keep the solution at 25° for three hours. The solution is clear; *extinction* of a 2-cm layer of the solution at 420 nm is not more than 0.1, Appendix 5.15 A.

Readily carbonisable substances : Dissolve 1.0 g in 20.0 ml of *sulphuric acid* (containing 94.5 to 95.5 per cent w/w of H_2SO_4), shaking vigorously, and keep the solution at 25° for exactly thirty minutes after adding the acid. The solution is clear; *extinction* of a 1-cm layer of the solution at 420 nm is not more than 0.1, Appendix 5.15 A.

Chloride : Boil 1 g with 30 ml of *water* for five minutes, cool and filter. To 10 ml of the filtrate add 1 ml of *dilute nitric acid* and 1 ml of *silver nitrate solution*; no opalescence is produced.

Sulphate : To 10 ml of the filtrate obtained in the test for *chloride* add 1 ml of *barium chloride solution*; no turbility is produced.

Heavy metals : Not more than 10 parts per million, determined on 2.0 g by Method B, Appendix 3.2.4.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying "in vacuo at 80°" for 4 hours, Appendix 5.8.

Assay : Weigh accurately about 0.5 g and dissolve in 25 ml of *acetone.* Add 10 drops of *bromothymol blue solution* and titrate with *0.1N sodium hydroxide* until a blue colour is obtained which persists for 15 seconds. Repeat the operation without the phenylbutazone; the difference between the two titrations represents the amount of alkali required by the phenylbutazone. Each ml of *0.1N sodium hydroxide* is equivalent to 0.03084 g of $C_{19}H_{20}N_2O_2$.

Storage : Store in well-closed containers.

Phenylbutazone Tablets

Category : Anti-inflammatory; analgesic.

Dose : Phenylbutazone, 100 to 600 mg daily, in divided doses.

Usual strengths : 100 mg and 200 mg.

Standards : Phenylbutazone Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Phenylbutazone, $C_{19}H_{20}N_2O_2$. The tablets are coated.

Identification : Extract a quantity of the powdered tablets equivalent to 0.2 g of Phenylbutazone with 40 ml of warm *acetone*, filter, and evaporate the filtrate to dryness. To 0.1 g of the residue add 1 ml of *glacial acetic acid* and 2 ml of *hydrochloric acid* and heat on a water-bath for thirty minutes. Cool, add 10 ml of *water* and filter. To the filtrate add 3 ml of *0.1M sodium nitrite*; a yellow colour is produced. Add 1 ml of this solution to 5 ml of *β-naphthol solution*; a brownish-red precipitate is produced which dissolves on the addition of *alcohol* producing a red solution.

Dissolution : Comply with the *dissolution test for tablets and capsules*, Appendix 5.7, using as the medium 1000 ml of a 0.68 per cent w/v solution of *potassium dihydrogen phosphate* adjusted to pH 7.5 by the addition of *N sodium hydroxide*, and placing one tablet in the basket for each test. Withdraw a sample of 10 ml of the medium and filter. Measure the *extinction* of a layer of suitable thickness of the filtered sample, suitably diluted, if necessary, at the maximum at about 264 nm, Appendix 5.15 A. Calculate the total content of $C_{19}H_{20}N_2O_2$ in the medium, taking 653 as the value of E(1 per cent, 1-cm) at the maximum at about 264 nm.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

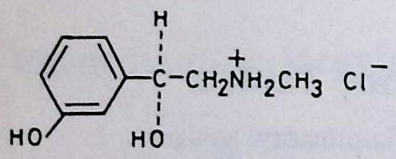
Digitized by Arya Samaj Foundation Chennai and eGangotri

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 0.5 g of Phenylbutazone and extract with 30, 30, 15 and 10 ml of warm *acetone*. Filter the combined extracts, cool, and titrate with *0.1N sodium hydroxide* using *bromothymol blue solution* as indicator and continuing the titration until a blue colour persisting for at least thirty seconds is obtained. Repeat the titration without the powdered tablets; the difference represents the amount of alkali required by the phenylbutazone. Each ml of *0.1N sodium hydroxide* is equivalent to 0.03084 g of $C_{19}H_{20}N_2O_2$.

Storage : Store in tightly-closed containers.

Phenylephrine Hydrochloride



$C_9H_{13}NO_2,HCl$ Mol.Wt. 203.67

Category : Adrenergic (vasopressor).

Dose : By subcutaneous or intramuscular injection, 5 mg; by intravenous injection, 0.5 mg.

Description : White or almost white, crystalline powder; odourless; taste, bitter.

Solubility : Freely soluble in *water* and in *alcohol*.

Standards : Phenylephrine Hydrochloride is (*S*)-*N*-[2-hydroxy-2-(3-hydroxyphenyl)ethyl]-*N*- methylammonium chloride. It contains not less than 98.5 per cent and not more than the equivalent of 102.5 per cent of $C_9H_{13}NO_2$, HCl, calculated with reference to the dried substance.

Identification : (A) Dissolve 10 mg in 1 ml of *water* and add 0.05 ml of *copper sulphate solution* and 1 ml of *sodium hydroxide solution*; a violet colour is produced. Add 1 ml of *solvent ether* and shake; the ether layer remains colourless.

(B) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.005 per cent w/v solution in *N sulphuric acid* exhibits a maximum only at 273 nm; *extinction* at 273 nm about 0.48, Appendix 5.15 A.

(C) Dissolve 0.3 g in 3 ml of *water* in a test-tube, add 1 ml of *dilute ammonia solution*, and scratch the tube to induce crystallisation; the crystals, after washing with ice-cold *water*, and drying at 105° for two hours, melt at about 170°, Appendix 5.11.

(D) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

Melting range : Between 141° and 144°, Appendix 5.11.

Specific optical rotation : Between −42° and −47.5°, determined in a 2 per cent w/v solution, Appendix 5.12.

Ketones : *Extinction* of a 1 cm layer of a 0.2 per cent w/v solution at 310 nm, not more than 0.2, Appendix 5.15 A.

Sulphate : 0.25 g complies with the *limit test for sulphates*, Appendix 3.2.8.

Sulphated ash : Not more than 0.2 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.5 g, dissolve in 30 ml of *glacial acetic acid*, add 10 ml of *mercuric acetate solution* and 0.1 ml of *crystal-violet solution*; titrate with *0.1N perchloric acid* to a blue-green end-point. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02037 g of $C_9H_{13}NO_2,HCl$.

Storage : Store in tightly-closed, light-resistant containers.

Phenylephrine Injection

Phenylephrine Hydrochloride Injection

Category : Adrenergic (vasopressor).

Dose : Phenylephrine Hydrochloride. By subcutaneous or intramuscular injection, 5 mg; by intravenous injection, 0.5 mg.

Usual strength : 10 mg in 1 ml.

Standards : Phenylephrine Injection is a sterile solution of Phenylephrine Hydrochloride in Water for Injection. It contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of $C_9H_{13}NO_2$, HCl.

Identification : (A) To a volume equivalent to 10 mg of Phenylephrine Hydrochloride, add, if necessary, sufficient *water* to produce 1 ml and then add 0.05 ml of *copper sulphate solution* and 1 ml of *sodium hydroxide solution*; a violet colour is produced. Add 1 ml of *solvent ether* and shake; the ether layer remains colourless.

(B) It gives the reactions of *chlorides*, Appendix 3.1.

pH : Between 4.0 and 6.5, Appendix 5.10.

Other requirements : Complies with the requirements stated under Injections.

Assay : To a volume equivalent to 50 mg of

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Phenylephrine Hydrochloride, add sufficient *N sulphuric acid* to produce 100.0 ml. Dilute 10.0 ml to 100.0 ml with *N sulphuric acid* and measure the *extinction* of the resulting solution at the maximum at about 273 nm, Appendix 5.15 A. Calculate the content of $C_9H_{13}NO_2$, HCl, taking 90 as the value of E(1 per cent, 1-cm) at the maximum at about 273 nm.

Storage : Store in single-dose or multiple-dose, light-resistant containers.

Phenylmercuric Acetate

$C_8H_8HgO_2$ Mol. Wt. 336.74

Category : Pharmaceutical aid (bacteriostatic).

Description : White to creamy-white, crystalline powder or small white prisms or leaflets; odourless or almost odourless.

Solubility : Slightly soluble in *water*; soluble in *alcohol* and in *acetone*.

Standards : Phenylmercuric Acetate contains not less than 98.0 per cent and not more than the equivalent of 100.5 per cent of $C_8H_8HgO_2$.

Identification : (A) To 5 ml of a saturated solution in *water* add 0.2 ml of *sodium sulphide solution*; a white precipitate is formed which turns black on boiling the mixture and allowing it to stand.

(B) To 0.1 g add 0.5 ml of *nitric acid*, warm gently until a dark brown colour is produced, and dilute with 10 ml of *water*; the odour of nitrobenzene is produced.

(C) To 0.1 g add 0.5 ml of *sulphuric acid* and 1 ml of *alcohol* and warm; the odour of ethyl acetate is produced.

Melting range : Between 149° and 153°, Appendix 5.11.

Mercuric salts and heavy metals : Shake 1.0 g with 10 ml of *dilute hydrochloric acid* and 40 ml of *water* for five minutes and filter, rejecting the first 10 ml of the filtrate; to 25 ml of the clear filtrate add 5 ml of *alcohol* and pass *hydrogen sulphide* through the solution. Any colour that develops is not deeper than that produced by passing *hydrogen sulphide* through a mixture of 25 ml of a 0.002 per cent w/v solution of *mercuric chloride* and 5 ml of *alcohol*.

Polymercurated benzene compounds : Not more than 1.5 per cent, determined by the following method: Shake about 2 g, accurately weighed, with 100 ml of *toluene* at 20°, filter, and wash the residue with successive portions of *toluene*, using a total of 50 ml; dry the residue at 105° for one hour and weigh.

Sulphated ash : Not more than 0.2 per cent, Appendix 3.2.7.

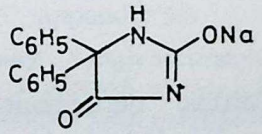
Assay : Weigh accurately about 0.3 g and boil with 5 ml of a 85 per cent w/v solution of *formic acid*, 15 ml of *water*, and 1 g of *zinc powder* under a reflux condenser for half an hour; wash the condenser with 10 ml of *water* and filter the combined solution and washings, retaining as much possible of the precipitate in the flask, and washing with *water* until the washings are neutral to *litmus paper*.

Re-attach the condenser to the flask, add 20 ml of *nitric acid* and 10 ml of *water*, boil for 10 minutes, wash the condenser with 10 ml of *water*, cool the flask, and use the solution in the flask to dissolve the precipitate retained on the filter; heat the solution on a water-bath for 3 minutes, add 0.5 g of *urea*, and sufficient *0.1N potassium permanganate* to produce a permanent pink colour, cool, add sufficient *hydrogen peroxide solution* to decolorise the solution, and titrate with *0.1N ammonium thiocyanate*, using *ferric ammonium sulphate solution* as indicator. Each ml of *0.1N ammonium thiocyanate* is equivalent to 0.01648 g of $C_8H_8HgO_2$.

Storage : Store in tightly-closed, light-resistant containers.

Phenytoin Sodium

Diphenylhydantoin Sodium



$C_{15}H_{11}N_2NaO_2$ Mol. Wt. 274.25

Category : Anticonvulsant.

Dose : 50 mg daily, increasing to 400 mg; by intramuscular or slow intravenous injection, upto 250 mg in accordance with the needs of the patient.

Description : White powder; odourless. Somewhat hygroscopic and on exposure to air gradually absorbs carbon dioxide with the liberation of diphenylhydantoin.

Solubility : Soluble in *water*, the solution showing some turbidity due to partial hydrolysis; soluble in *alcohol*; practically insoluble in *chloroform* and in *solvent ether*.

Standards : Phenytoin Sodium is the sodium derivative of 5,5-diphenylionidazolidine-2,4-dione. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_{15}H_{11}N_2NaO_2$, calculated with reference to the dried substance.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Identification : (A) Shake 100 mg with 20 ml of *water*, acidify with *dilute hydrochloric acid*, and extract with 10 ml of *chloroform*; wash the chloroform extract with *water* and evaporate to dryness. The residue melts between 292° and 299°, Appendix 5.11.

(B) Dissolve 0.25 g in 5 ml of *water* and acidify with *dilute hydrochloric acid*; a white precipitate is produced.

(C) Incinerate 0.1 g; the residue gives the reactions of *sodium*, Appendix 3.1.

(D) Dissolve 0.1 g in 10 ml of a 10 per cent w/v solution of *pyridine*, add 1 ml of *copper sulphate with pyridine solution*, and allow to stand for ten minutes; a blue precipitate is produced.

Clarity and colour of solution : 20 ml of a 5.0 per cent w/v solution requires not more than 4 ml of *0.1N sodium hydroxide* to produce a clear, colourless solution.

Heavy metals : Not more than 20 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

Loss on drying : Not more than 3.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.4 g and carry out the **Assay** described under Phenobarbitone Sodium. Each ml of *0.1N perchloric acid* is equivalent to 0.02743 g of $C_{15}H_{11}N_2NaO_2$.

Storage : Store in well-closed containers.

Phenytoin Injection

Category : Anticonvulsant; Cardiac depressant (anti-arrhythmic).

Dose : Anticonvulsant—By slow intravenous injection, 150 to 250 mg, then 0.1 to 0.15 g repeated in thirty minutes.

Cardiac depressant—By intravenous injection, 50 to 100 mg, repeated every ten to fifteen minutes.

Usual strengths : 100 mg and 250 mg.

Standards : Phenytoin Injection is a sterile solution of Phenytoin Sodium in Water for Injection or other suitable solvents. It is prepared by dissolving the content of a sealed container in the solvent shortly before use. The sealed container contains not less than 90.0 per cent and not more than 115.0 per cent of the stated amount of $C_{15}H_{11}N_2NaO_2$.

The contents of the sealed container comply with the following requirements:

Description; Identification; Clarity and colour of solution; Heavy metals; Loss on drying; Assay : Comply with the requirements stated under Phenytoin Sodium.

Completeness of solution : It dissolves in the solvent and in the concentration recommended on the label, to give a clear solution.

pH : Between 10.0 and 12.0, Appendix 5.10, determined in a 5.0 per cent w/v solution prepared in the solvent and as directed on the label.

Uniformity of weight : Complies with the requirements for **Uniformity of weight**, test (2) stated under Injections.

Other requirements : Complies with the requirements stated under Injections.

Storage : Store in sealed container in a dry, cool place. The Injection should be used immediately after preparation.

Labelling : The label on the container states (1) Phenytoin Sodium for Injection; (2) the quantity of Phenytoin Sodium contained in it; (3) the directions for preparing the Injection; (4) the conditions of storage.

Phenytoin Sodium Tablets

Phenytoin Tablets; Soluble Phenytoin Tablets; Diphenylhydantoin Tablets

Category : Anticonvulsant.

Dose : Phenytoin Sodium, 50 mg daily, increasing to 400 mg, in accordance with the needs of the patient.

Usual strength : 100 mg.

Standards : Phenytoin Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Phenytoin Sodium, $C_{15}H_{11}N_2NaO_2$. The tablets are coated.

Identification : (A) Triturate a quantity of the powdered tablets equivalent to 100 mg of Phenytoin Sodium with 10 ml of *water* and filter; the filtrate yields a white precipitate on the addition of *dilute hydrochloric acid*.

(B) Shake a quantity of the powdered tablets equivalent to 100 mg of Phenytoin Sodium with 20 ml of *water*, acidify with *dilute hydrochloric acid*, and extract with *chloroform*, wash the *chloroform* extract with *water* and evaporate to dryness. The residue melts at about 293°, Appendix 5.11.

(C) The powdered tablets give the reactions of *sodium*, Appendix 3.1.

Other requirements : Comply with the requirements stated under Tablets.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

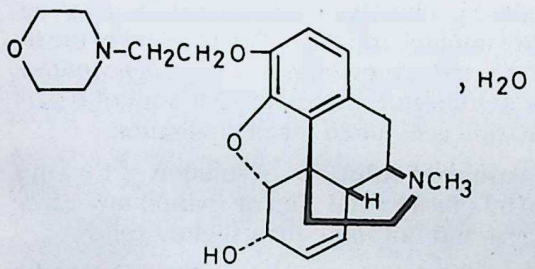
Digitized by Arya Samaj Foundation Chennai and eGangotri

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 0.25 g of Phenytoin Sodium, shake with 40 ml of *0.01N sodium hydroxide* for five minutes and add sufficient *0.01N sodium hydroxide* to produce 50.0 ml. Centrifuge, acidify 25.0 ml of the clear liquid with 10 ml of *0.1N hydrochloric acid*, and extract successively with 50, 40 and 25 ml of *solvent ether*. Wash the combined extracts with 10 ml of *water*, evaporate to dryness, and dry the residue at 105°. Dissolve in 50 ml of *pyridine* and titrate with *0.1N tetrabutylammonium hydroxide*, using a 0.3 per cent w/v solution of *thymol blue* in *pyridine* as indicator and taking care to prevent absorption of carbon dioxide from the atmosphere. Perform a blank determination and make any necessary correction. Each ml of *0.1N tetrabutylammonium hydroxide* is equivalent to 0.02743 g of $C_{15}H_{11}N_2NaO_2$.

Storage : Store in tightly-closed containers.

Pholcodine

Pholcodinum



$C_{23}H_{30}N_2O_4, H_2O$ Mol. Wt. 416.51

Category : Cough suppressant.

Dose : Upto 60 mg daily, in divided doses.

Description : White or almost white, crystalline powder; odourless; taste, very bitter.

Solubility : Sparingly soluble in *water*; freely soluble in *ethyl alcohol*; slightly soluble in *solvent ether*; very soluble in *chloroform*, and in *acetone*; soluble in *dilute hydrochloric acid*.

Standards : Pholcodine is the monohydrate of O^3-(2-morpholinoethyl) morphine. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_{23}H_{30}N_2O_4$, calculated with reference to the dried substance.

Identification : (A) The light absorption, in the range 240 to 350 nm, of a 1-cm layer of a 0.01 per cent w/v solution in *0.1N hydrochloric acid* exhibits a maximum only at 283 nm, *extinction* at 283 nm, about 0.40, Appendix 5.15 A.

(B) To 20 ml of a 0.05 per cent w/v solution, add 65 ml of *water*, 10 ml of *N sodium hydroxide*, and sufficient *water* to produce 100 ml. The light absorption, in the range 240 to 350 nm of a 1-cm layer of the resulting solution exhibits maximum only at 284 nm; *extinction* at 284 nm, about 0.38, Appendix 5.15 A.

(C) Dissolve 50 mg in 1 ml of *sulphuric acid* and add 0.05 ml of *ammonium molybdate solution*; a pale blue colour is produced; the colour changes to deep blue on warming. Add 0.05 ml of *dilute nitric acid*, the colour changes to brownish red.

Melting range : About 99°, after sintering at about 95°, Appendix 5.11.

Specific optical rotation : Between −94° and −98°, determined on a 2.0 per cent w/v solution in *alcohol*, Appendix 5.12.

Morphine : Dissolve 0.1 g in 5 ml of *0.1N hydrochloric acid*, add 2 ml of a 1 per cent w/v solution of *sodium nitrite*, allow to stand for 15 minutes and add 3 ml of *dilute ammonia solution*; the yellow colour of the solution is not deeper than that obtained when 5 ml of a 0.002 per cent w/v solution of *anhydrous morphine* in *0.1N hydrochloric acid* is treated exactly in the same manner.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not less than 3.9 and not more than 4.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.5 g and dissolve in 20 ml of *glacial acetic acid*. Add *crystal-violet solution* and titrate with *0.1N perchloric acid* to green end-point. perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.01993 g of $C_{23}H_{30}N_2O_4$.

Storage : Store in well-closed containers.

Phosphoric Acid

Orthophosphoric Acid; Concentrated Phosphoric Acid

H_3PO_4 Mol. Wt. 98.00

Category : Pharmaceutical aid (solvent).

Description : Clear and colourless syrupy liquid. Corrosive.

Solubility : Miscible with *water* and with *alcohol*.

Standards : Phosphoric Acid contains not less than 85.0 per cent w/w and not more than 90.0 per cent w/w of H_3PO_4.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Identification : (A) Dilute with *water*. The resulting solution is strongly acid.

(B) A solution (1 in 10) gives the reactions of *phosphates*, Appendix 3.1.

Clarity and colour of solution : 10 g diluted with sufficient *water* to produce 150 ml gives a clear and colourless solution.

Hypophosphorous and phosphorous acids : To 0.5 ml add 10 ml of *water* and 2 ml of *silver nitrate solution* and heat on a water-bath for five minutes; the solution shows no change in appearance.

Alkali phosphates : To 1 ml in a graduated cylinder add 6 ml of *solvent ether* and 2 ml of *alcohol*; no turbidity is produced.

Chloride : 1 ml complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphate : 0.5 ml complies with the *limit test for sulphates*, Appendix 3.2.8.

Arsenic : Not more than 2 parts per million, Appendix 3.2.1.

Heavy metals : Not more than 10 parts per million, determined by Method A on a solution prepared by diluting 1.2 ml with 10 ml of *water*, neutralising with *dilute ammonia solution*, adding sufficient *dilute acetic acid* to render the solution acidic and finally diluting to 25 ml with *water*, Appendix 3.2.4.

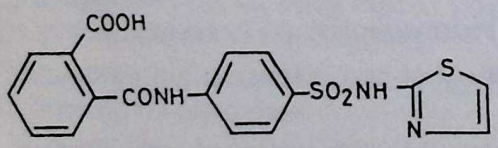
Iron : 0.1 ml complies with the *limit test for iron*, Appendix 3.2.5.

Aluminium and calcium : To 1 ml add 10 ml of *water* and 8 ml of *dilute ammonia solution*; the solution remains clear.

Assay : Weigh accurately about 1 g and mix with a solution of 10 g of *sodium chloride* in 30 ml of *water*. Titrate with *N sodium hydroxide*, using *phenolphthalein solution* as indicator. Each ml of *N sodium hydroxide* is equivalent to 0.049 g of H_3PO_4.

Storage : Store in well-closed glass containers.

Phthalylsulphathiazole



$C_{17}H_{13}N_3O_5S_2$ Mol. Wt. 403.43

Category : Antibacterial (intestinal).

Dose : 5 to 10 g daily, in divided doses.

Description : White or yellowish-white crystals or powder; odourless or almost odourless; taste, slightly bitter.

Solubility : Phthalylsulphathiazole is 4'-(2-thiazolylsulphamoyl) phthalanilic acid. It contains not less than 98.5 per cent and not more than the equivalent of 102.5 per cent of $C_{17}H_{13}N_3O_5S_2$. Calculated with reference to the dried substance.

Identification : (A) When strongly heated, pungent vapours are evolved which blacken *lead acetate paper*.

(B) Boil 2 g with 20 ml of *sodium hydroxide solution* for ten minutes, cool, add 15 ml of *hydrochloric acid* and slowly add *sodium bicarbonate solution* until no more carbon dioxide is evolved and a white precipitate forms; the precipitate, after recrystallisation from *water* and drying at 105°, melts between 198° and 202°, Appendix 5.11.

(C) Heat 0.1 g with 50 mg of *resorcinol* and 1 ml of *sulphuric acid* for about one minute, cool, pour into *water* and make alkaline with *sodium hydroxide solution*; the solution obtained shows a distinct green fluorescence. The fluorescence disappears when the solution is made acidic but reappears when it is made alkaline.

Acidity : Shake 2 g with 100 ml of *water* at room temperature for thirty minutes and filter. Titrate 25 ml of the filtrate with *0.02N sodium hydroxide* using *phenolphthalein solution* as indicator; not more than 5 ml of *0.02N sodium hydroxide* is required for neutralisation.

Clarity and colour of solution : A solution of 1.0 g in a mixture of 20 ml of *water* and 1 ml of *sodium hydroxide solution* is clear and not more than slightly yellow.

Arsenic : Not more than 2 parts per million, Appendix 3.2.1.

Heavy metals : Not more than 20 parts per million, determined by the method described under Succinylsulphathiazole, Appendix 3.2.4.

Iron : Ignite 1.0 g with 1 g of *anhydrous sodium carbonate*, cool, dissolve the residue in 15 ml of *dilute hydrochloric acid*; the solution complies with the *limit test for iron*, Appendix 3.2.5.

Chloride : Heat 4.0 g with 200 ml of *water* at 70° for five minutes, cool and filter; 50 ml of the filtrate complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphate : A second 50-ml portion of the filtrate obtained in the test for **Chloride** complies with the *limit test for sulphates*, Appendix 3.2.8.

Free sulphathiazole : Dissolve 0.5 g in a mixture of 12.5 ml of *N sodium hydroxide* and 12.5 ml of *water* and add sufficient *water* to produce 500 ml. Mix 4.5 ml of *N hydrochloric acid*, 3 ml of *water*, 10 ml of a 2.5 per cent w/v solution of *dimethylaminobenzaldehyde* in *alcohol*, add 2 ml of a solution prepared by dissolving 39.4 g of *citric acid* in 188 ml of *2N sodium hydroxide* and diluting to 250 ml with *water*. Cool to 20°, add 1 ml of the

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

solution of phthalylsulphathiazole, dilute to 25 ml with *water* and set aside for ten minutes at 20°. The *extinction* of a 1-cm layer of the resulting solution at about 455 nm is not greater than that of a solution prepared in the same manner using 25 mg of *sulphathiazole* in place of the substance being examined, Appendix 5.15 A.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel H* as the coating substance and a mixture of 15 volumes of *n-butyl alcohol* and 3 volumes of *N ammonia* as the mobile phase. Apply separately to the plate 10 µl of each of three solutions in a mixture of 9 volumes of *alcohol* and 1 volume of *strong ammonia solution* containing: (1) 1.0 per cent w/v of the substance being examined; (2) 0.005 per cent w/v of *sulphanilamide R.S.* and (3) 0.05 per cent w/v of *sulphathiazole*. After removal of the plate, heat it at 105° for ten minutes and spray with a 0.1 per cent w/v solution of *dimethylaminobenzaldehyde* in *alcohol* containing 1 per cent v/v of *hydrochloric acid*. Any spot in the chromatogram obtained with solution (1), other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (2); disregard any spot corresponding to the spot in the chromatogram obtained with solution (3).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 2.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.5 g and heat on a water-bath for two hours with 10 ml of *sodium hydroxide solution*, cool, add 10 ml of *water* and 20 ml of *hydrochloric acid*, and carry out the *nitrite titration*, Appendix 3.3.4. Each ml of *0.1M sodium nitrite* is equivalent to 0.04034 g of $C_{17}H_{13}N_3O_5S_2$.

Storage : Store in well-closed, light-resistant containers.

Phthalylsulphathiazole Tablets

Category : Antibacterial (intestinal).

Dose : Phthalylsulphathiazole, 5 to 10 g daily, in divided doses.

Usual strength : 0.5 g.

Standards : Phthalylsulphathiazole Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Phthalylsulphathiazole, $C_{17}H_{13}N_3O_5S_2$.

Identification : Extract a quantity of the powdered tablets equivalent to about 0.5 g Phthalylsulphathiazole with hot *acetone* and evaporate the extract to dryness. The residue after drying at 105°C, complies with **Identification** tests (A) and (C) described under Phthalylsulphathiazole and with the following test: To 10 mg add 20 mg of *phenol* and 3 drops of *sulphuric acid*, heat until the solution becomes brown, cool, add 20 ml of *water*, and make alkaline with *sodium hydroxide solution*: a pink colour is produced (distinction from succinylsulphathiazole).

Free sulphathiazole : Dissolve a quantity of the powdered tablets equivalent to 0.5 g of Phthalylsulphathiazole as completely as possible in a mixture of 12.5 ml of *N sodium hydroxide* and 12.5 ml of *water*, add sufficient *water* to produce 500 ml and filter. Complete the test described under Phthalylsulphathiazole, beginning at the words "Mix 4.5 ml .....".

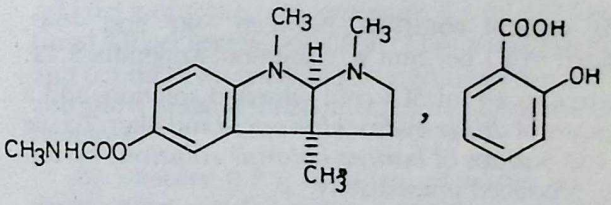
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh 20 tablets and reduce to a *fine powder*. Weigh accurately a portion of the powder equivalent to about 1 g of Phthalylsulphathiazole and transfer to a small flask. Add 20 ml of *hydrochloric acid* and 10 ml of *water*, and heat under a reflux condenser for one hour. Completely transfer the liquid to a suitable beaker with the aid of 20 to 25 ml of *dilute hydrochloric acid*. Carry out the *nitrite titration*, Appendix 3.3.4. Each ml of *0.1M sodium nitrite* is equivalent to 0.04034 g of $C_{17}H_{13}N_3O_5S_2$.

Storage : Store in well-closed, light-resistant containers.

Physostigmine Salicylate

Eserine Salicylate



$C_{15}H_{21}N_3O_2, C_7H_6O_3$ Mol. Wt. 413.47

Category : Anticholinesterase.

Dose : 0.6 to 1.2 mg.

Description : Colourless or faintly yellow crystals, turning red gradually under the action of air and light and rapidly in presence of moisture; odourless.

Solubility : Sparingly soluble in *water*; soluble in *alcohol*, freely soluble in *chloroform* and slightly soluble in *solvent ether*.

Standards : Physostigmine Salicylate is the monosalicylate of (3a*S*,8a*R*)-1,2,3,3a,8,8a-hexahydro-1,3a,8-trimethylpyrrolo (2,3-b) indol-5-ylmethylcar-

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

bamate. It contains not less than 98.5 per cent of $C_{15}H_{21}N_3O_2$, $C_7H_6O_3$, calculated with reference to the dried substance.

Identification : (A) To a 1.0 per cent w/v solution add *N sodium hydroxide*; a white precipitate, which turns pink is produced; the precipitate dissolves in an excess of the reagent, producing a red solution.

(B) Warm a few mg with several drops of *dilute ammonia solution*; a yellowish-red solution is produced; evaporate this solution; a bluish residue is produced. Dissolve a portion of the residue in *alcohol* and add *acetic acid*; a blue solution with a red fluorescence is formed which is intensified by dilution with *water*. Dissolve another portion of the residue in *sulphuric acid*; a green solution is formed which on the gradual addition of *alcohol* changes to red but reverts to green when the alcohol is evaporated.

(C) A solution in *water* gives a violet colour with *ferric chloride solution*, which persists after addition of *dilute acetic acid* or *alcohol*.

(D) 15 ml of a 1 per cent w/v solution to which a few drops of *hydrochloric acid* have been added, gives a precipitate which after washing and drying, melts at about 158°, Appendix 5.11.

Melting range : Between 184° and 187°, Appendix 5.11.

Acidity : A 1.0 per cent w/v solution is neutral to *methyl red solution*.

Clarity and colour of solution : A 1.0 per cent w/v solution is clear and colourless.

Readily carbonisable substances : To 0.1 g add 5 ml of *sulphuric acid*; any colour which develops within five minutes is not more intense than a mixture of 0.6 ml of *ferric chloride C.S.*, 0.15 ml of *cobalt chloride C.S.* and 4.25 ml of *hydrochloric acid (1 per cent w/v)*.

Specific optical rotation : Between −90° and −94°, determined in a 1 per cent w/v solution, Appendix 5.12.

Sulphate : To 10 ml of a cold saturated solution, add a slight excess of *dilute hydrochloric acid* and filter. To the filtrate add 5 drops of *barium chloride solution*; no turbidity is produced immediately.

Eserdine : To 5 ml of a 1 per cent w/v solution add a few crystals of *potassium iodate* and one drop of *dilute hydrochloric acid*. Add 2 ml of *chloroform* and shake. The chloroform layer does not turn violet within one minute.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.2 g and dissolve in 15 ml of a mixture of equal volumes of *chloroform* and *glacial acetic acid*. Titrate with *0.1N perchloric acid*, determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.04135 g of $C_{15}H_{21}N_3O_2$, $C_7H_6O_3$.

Storage : Store in tightly-closed, light-resistant containers.

Physostigmine Injection

Physostigmine Salicylate Injection

Category : Anticholinesterase.

Dose : Physostigmine Salicylate. By subcutaneous injection, 0.6 to 1.2 mg.

Usual strength : 0.6 mg per ml.

Standards : Physostigmine Injection is a sterile solution of Physostigmine Salicylate in Water for Injection. It contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of $C_{22}H_{27}N_3O_5$.

Identification : Complies with **Identification** tests (A), (C) and (D) described under Physostigmine Salicylate.

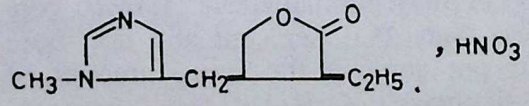
pH : Between 4.0 and 6.0, Appendix 5.10.

Other requirements : Complies with the requirements stated under Injections.

Assay : Measure accurately a volume equivalent to about 30 mg of Physostigmine Salicylate in a separator, add about 0.25 g of *sodium bicarbonate* and extract with six quantities, each of 15 ml, of *chloroform*. Filter the combined chloroform extracts through about 10 g of *anhydrous sodium sulphate*. Add 25 ml of *glacial acetic acid* to the filtrate and titrate with *0.01N perchloric acid*, determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.01N perchloric acid* is equivalent to 0.004135 g of $C_{22}H_{27}N_3O_5$.

Storage : Store in single-dose, light-resistant glass containers.

Pilocarpine Nitrate



$C_{11}H_{16}N_2O_2$, HNO_3 Mol. Wt. 271.27

Category : Cholinergic (ophthalmic).

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Description : Colourless crystals or white crystalline powder; odourless or with a slight odour.

Solubility : Freely soluble in *water*; sparingly soluble in *alcohol*; practically insoluble in *chloroform* and in *solvent ether*.

Standards : Pilocarpine Nitrate is the nitrate of (3*S*,4*R*)-ethyldihydro-4-[(1-methyl-1*H*-imidazole-5-yl)methyl]-furan-2(3*H*)-one. It contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of $C_{11}H_{16}N_2O_2, HNO_3$, calculated with reference to the dried substance.

Identification : (A) Dissolve about 10 mg in 2 ml of *water*, add 2 drops of a 5 per cent w/v solution of *potassium dichromate*, 1 ml of *hydrogen peroxide solution* and 2 ml of *chloroform* and shake. The chloroform layer turns violet.

(B) A solution (1 in 20) gives the reactions of *nitrates*, Appendix 3.1.

(C) It melts at about 176°, with decomposition, Appendix 5.11.

Specific optical rotation : Between +79.5° and +83°, determined in a 5.0 per cent w/v solution, Appendix 5.12.

Acidity : A 1 per cent w/v solution gives a red colour with *methyl red solution* and a blue colour with *bromophenol blue solution*.

Other alkaloids : To a 1.0 per cent w/v solution, add *dilute ammonia solution*; no turbidity is produced. To a 1.0 per cent w/v solution, add a few drops of *potassium dichromate solution*; no turbidity is produced.

Chloride : To 5 ml of a 2 per cent w/v solution acidified with *nitric acid*, add a few drops of *silver nitrate solution*; no opalescence is produced immediately.

Readily carbonisable substances : Dissolve 10 mg in 1 ml of *sulphuric acid*. The solution remains colourless, even after adding 10 drops of *nitric acid*.

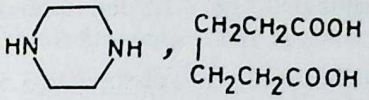
Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 2.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.2 g and dissolve in 50 ml of *glacial acetic acid*. Titrate with *0.1N perchloric acid*, determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02713 g of $C_{11}H_{16}N_2O_2, HNO_3$.

Storage : Store in tightly-closed, light-resistant containers.

Piperazine Adipate



$C_4H_{10}N_2, C_6H_{10}O_4$ Mol. Wt. 232.28

Category : Anthelmintic (for threadworm and roundworm infestation).

Dose : For an adult; in the treatment of threadworm infestation, 1 to 2 g daily, in divided doses. In the treatment of roundworm infestation, 4.5 g as a single dose.

For a child; in the treatment of threadworm infestation, the equivalent of 40 mg of piperazine hexahydrate per kg of body weight daily, in divided doses. In the treatment of roundworm infestation, as a single dose, the equivalent of 120 mg of piperazine hexahydrate per kg of body weight upto a maximum dose of 4 g.

144 mg of Piperazine Adipate is approximately equivalent to 120 mg of piperazine hexahydrate.

Description : White, crystalline powder; odourless; taste, slightly acid.

Solubility : Soluble in *water*; practically insoluble in *alcohol*.

Standards : Piperazine Adipate is the adipic acid salt of piperazine. It contains not less than 98.0 per cent of $C_4H_{10}N_2, C_6H_{10}O_4$, calculated with reference to the dried substance.

Identification : (A) Dissolve 0.1 g in 5.0 ml of *water*. Add 0.5 g of *sodium bicarbonate*, 0.5 ml of a freshly prepared 5.0 per cent w/v solution of *potassium ferricyanide* and 0.1 ml of *mercury*, shake vigorously for one minute, and allow to stand for 20 minutes; a reddish colour slowly develops.

(B) Dissolve 0.5 g in 10 ml of *water*, add 5 ml of *hydrochloric acid* and extract with three quantities, each of 10 ml, of *solvent ether*, evaporate the combined ether extracts to dryness; the residue after washing with a small volume of *water* and drying at 105°, melts at about 152°, Appendix 5.11.

(C) It melts at about 250° with decomposition, Appendix 5.11.

pH : Between 5.0 and 6.0, determined in a 5.0 per cent w/v solution, Appendix 5.10.

Heavy metals : Not more than 20 parts per million, determined by Method A, on a solution prepared by dissolving 1.0 g in 20 ml of *water*, 0.5 ml of *0.1N hydrochloric acid* and sufficient *water* to produce 25 ml, Appendix 3.2.4.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.2 g and dissolve in 3.5 ml of *N sulphuric acid* and 10 ml of *water*, add 100 ml of *picric acid solution*, heat on a water-bath for fifteen minutes and allow to stand for one hour. Filter through a sintered-glass crucible (grade-4 porosity) and wash the residue with successive quantities, each of 10 ml, of a mixture of equal volumes of a saturated solution of *picric acid* and *water* until the washings are free from sulphate. Finally, wash with five quantities, each of 10 ml, of *alcohol* and dry the residue to constant weight at 105°. Each g of residue is equivalent to 0.4268 g of $C_4H_{10}N_2, C_6H_{10}O_4$.

Storage : Store in well-closed containers.

Piperazine Adipate Tablets

Category : Anthelmintic (for threadworm and roundworm infestation).

Dose : Piperazine Adipate, for an adult, in the treatment of threadworm infestation, 1 to 2 g daily in divided doses; in the treatment of roundworm infestation, 4.5 g as a single dose.

For a child; in the treatment of threadworm infestation, the equivalent of 40 mg of piperazine hexahydrate per kg of body weight daily, in divided doses; in the treatment of roundworm infestation as a single dose, the equivalent of 120 mg of piperazine hexahydrate per kg of body weight upto a maximum of 4 g.

144 mg of Piperazine Adipate is approximately equivalent to 120 mg of piperazine hexahydrate.

Usual strength : 300 mg.

Standards : Piperazine Adipate Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Piperazine Adipate, $C_4H_{10}N_2, C_6H_{10}O_4$.

Identification : (A) Extract a quantity of the powdered tablets equivalent to 1 g of Piperazine Adipate with 20 ml of *water* and filter. 1 ml of the filtrate diluted to 5 ml with *water* complies with **Identification** test (A) described under Piperazine Adipate.

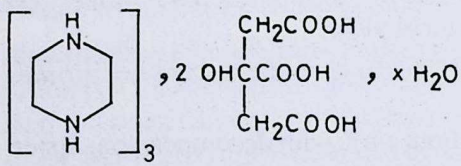
(B) 10 ml of the filtrate complies with **Identification** test (B) described under Piperazine Adipate.

Disintegration : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.2 g of Piperazine Adipate, shake with 10 ml of *water* for one hour, filter, and wash the residue with 2 quantities, each of 10 ml, of *water*. To the combined extract and washings, add 5 ml of *sulphuric acid* and 50 ml of *picric acid solution*, bring to boil, allow to stand for several hours and complete the **Assay** described under Piperazine Adipate, beginning at the words "Filter through a sintered glass crucible.....".

Storage : Store in well-closed containers.

Piperazine Citrate



$(C_4H_{10}N_2)_3, 2C_6H_8O_7$ Mol. Wt. 642.66 (anhydrous)

Category : Anthelmintic.

Dose : For threadworms, 0.6 to 4.5 g daily, in divided doses. For roundworms, upto 5 g in a single dose, according to the age of the patient.

NOTE – 100 mg of Piperazine Citrate is approximately equivalent to 80 mg of Piperazine Hydrate.

Description : White crystalline powder, almost odourless; taste, acid.

Solubility : Freely soluble in *water*, practically insoluble in *alcohol*.

Standards : Piperazine Citrate is piperazine citrate containing a variable amount of water of crystallisation corresponding to five or six molecules of water. It contains not less than 98.0 per cent of $(C_4H_{10}N_2)_3, 2C_6H_8O_7$, calculated with reference to the anhydrous substance.

Identification : (A) Dissolve about 40 mg in 1 ml of *water*, add 2 ml of a 20 per cent w/v solution of *trichloroacetic acid* in *alcohol* and mix. The precipitate, after washing with *alcohol*, and drying by suction, has a melting range between 115° and 121°, Appendix 5.11.

(B) A solution (1 in 20) gives the reactions of *citrates*, Appendix 3.1.

(C) It melts at about 190°, Appendix 5.11, the determination being done after drying at 105° for two hours.

pH : Between 5.0 and 6.0, determined in a 5 per cent w/v solution, Appendix 5.10.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Primary amines and ammonia : Dissolve 0.5 g in 10 ml of *water*. Add 0.5 ml of *sodium hydroxide solution*, 1 ml of *acetone* and 1 ml of *sodium nitroprusside solution*. Mix and allow to stand for exactly ten minutes. Determine the *extinction* of this solution at 520 nm and at 600 nm using a blank consisting of the same quantities of the same reagents, but substituting *water* for *sodium hydroxide solution*. The ratio of the *extinction* at 600 nm to that at 520 nm is not more than 0.50, equivalent to about 0.7 per cent of primary amines and ammonia, Appendix 5.15 A.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

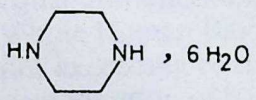
Water : Between 10.0 per cent and 15.0 per cent w/w, Appendix 3.3.25.

Assay : Weigh accurately about 0.2 g and dissolve in 100 ml of *glacial acetic acid*, warming if necessary. Cool and titrate with *0.1N perchloric acid* in *dioxan*, using *crystal-violet solution* as indicator. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.01071 g of $(C_4H_{10}N_2)_3, 2C_6H_8O_7$.

Storage : Store in well-closed, light-resistant containers.

Piperazine Hydrate

Piperazine



$C_4H_{10}N_2, 6H_2O$ Mol. Wt. 194.23

Category : Anthelmintic (for threadworms and roundworms)

Dose : In roundworm (Ascaris) infestation—adults, 4 g as a single dose; children, 120 mg per kg of body weight to a maximum of 4 g, as a single dose.

In threadworm infestation—adults, 1 to 2 g daily, in divided doses; children, 40 mg per kg of body weight daily, in divided doses.

Description : Colourless, glassy crystals; odour, faint and characteristic; deliquescent.

Solubility : Freely soluble in *water* and in *alcohol*; insoluble in *solvent ether*.

Standards : Piperazine Hydrate contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_4H_{10}N_2, 6H_2O$.

Identification : (A) Complies with **Identification** test (A) described under Piperazine Adipate.

(B) Dissolve 0.2 g in 5 ml of *dilute hydrochloric acid*, add 0.5 g *sodium nitrite* and heat to boiling. Cool in ice for fifteen minutes scratching the walls of the container with a glass rod. Filter. The crystals, after washing with 10 ml of ice-cold *water* and drying at 105°, melt at about 159°, Appendix 5.11.

Melting range : Between 43° and 45°, Appendix 5.11.

Colour of solution : Dissolve 20.0 g in sufficient *water* to produce 50.0 ml; the resulting solution is no more coloured than 2.0 ml of *ferric chloride C.S.* diluted to 50.0 ml with *water*.

Primary amines : Not more than 0.7 per cent, determined in the following manner: Dissolve 0.2 g in 10 ml of *water*, add 1 ml of *acetone* and 0.5 ml of a freshly prepared 10.0 per cent w/v solution of *sodium nitroprusside*, mix and allow to stand for exactly ten minutes. Measure the *extinction* of the resulting solution at 520 nm and at 600 nm, Appendix 5.15 A, using a reagent blank as the reference solution. The ratio of the *extinction* at 600 nm to the *extinction* at 520 nm does not exceed 0.5.

Heavy metals : Not more than 20 parts per million, determined on 1.0 g by Method A, Appendix 3.2.4.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Assay : Carry out the **Assay** described under Piperazine Adipate. Each g of residue is equivalent to 0.3567 g of $C_4H_{10}N_2, 6H_2O$.

Storage : Store in tightly-closed, light-resistant containers.

Piperazine Phosphate

$C_4H_{10}N_2, H_3PO_4, H_2O$ Mol. Wt. 202.15

Category : Anthelmintic (intestinal threadworms and roundworms).

Dose : For an adult, in the treatment of threadworm infestation, 1 to 2 g daily, in divided doses; in the treatment of roundworm infestation, 4.5 g as a single dose.

For a child, in the treatment of threadworm infestation, the equivalent of 40 mg of Piperazine Hydrate per kg of body weight daily, in divided doses; in the treatment of roundworm infestation, as a single dose, the equivalent of 120 mg of Piperazine Hydrate per kg of body weight upto a maximum dose of 4 g.

NOTE – 125 mg of Piperazine Phosphate is approximately equivalent to 120 mg of Piperazine Hexahydrate.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Description : White, crystalline powder; odourless; taste, slightly acid.

Solubility : Sparingly soluble in *water*; practically insoluble in *alcohol*.

Standards : Piperazine Phosphate is the monohydrate of the orthrophosphoric acid salt of piperazine. It contains not less than 98.5 per cent of $C_4H_{10}N_2$, H_3PO_4, calculated with reference to the anhydrous substance.

Identification : (A) Complies with **Identification** test (A) described under Piperazine Adipate.

(B) Dissolve 0.2 g in 5 ml of *dilute hydrochloric acid*, add with stirring 1 ml of a 50 per cent w/v solution of *sodium nitrite* and cool in ice for fifteen minutes, stirring if necessary to induce crystallisation; the crystals after washing with 10 ml of cold *water* and drying at 105°, melt at about 159°, Appendix 5.11.

(C) A solution (1 in 20) gives the reactions of *phosphates*, Appendix 3.1.

pH : Between 6.0 and 6.5, determined in a 1.0 per cent w/v solution, Appendix 5.10.

Heavy metals : Not more than 20 parts per million determined by Method A on a solution prepared by dissolving 2.0 g in a mixture of 46 ml of *water*, and 4 ml of *0.1N hydrochloric acid*, filtering and using 25 ml of the filtrate, Appendix 3.2.4.

Water : Between 8.0 per cent and 9.5 per cent w/w, Appendix 3.3.25.

Assay : Carry out the **Assay** described under Piperazine Adipate. Each g of residue is equivalent to 0.3382 g of $C_4H_{10}N_2, H_3PO_4$.

Storage : Store in well-closed containers.

Piperazine Phosphate Tablets

Category : Anthelmintic (intestinal threadworm and roundworm infestation).

Dose : Piperazine Phosphate, for an adult in the treatment of threadworm infestation, 1 to 2 g daily, in divided doses; in the treatment of roundworm infestation, 4.5 g as a single dose.

For a child, in the treatment of threadworm infestation the equivalent of 40 mg of Piperazine Hydrate per kg of body weight daily, in divided doses; in the treatment of roundworm infestation as a single dose, the equivalent of 120 mg of Piperazine Hydrate per kg of body weight upto a maximum dose of 4 g.

NOTE – 260 mg of Piperazine Phosphate is equivalent to 250 mg of Piperazine Hexahydrate.

Usual strengths : 260 mg; 520 mg.

Standards : Piperazine Phosphate Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Piperazine Phosphate, $C_4H_{10}N_2, H_3PO_4, H_2O$.

Identification : (A) Extract a quantity of the powdered tablets equivalent to 1 g of Piperazine Phosphate with 20 ml of *water* and filter. One ml of the filtrate diluted to 5 ml with *water* complies with **Identification** test (A) described under Piperazine Adipate.

(B) A mixture of 4 ml of the filtrate obtained in **Identification** test (A) and 1 ml of *hydrochloric acid* complies with **Identification** test (B) described under Piperazine Phosphate.

(C) The filtrate obtained in **Identification** test (A) gives the reactions of *phosphates*, Appendix 3.1.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.15 g of Piperazine Phosphate and complete the **Assay** described under Piperazine Adipate Tablets, beginning at the words "Shake with 10 ml of *water*.....". Each g of residue is equivalent to 0.3714 g of $C_4H_{10}N_2, H_3PO_4, H_2O$.

Storage : Store in tightly-closed containers.

Plague Vaccine

Formolised Plague Vaccine

Category : Active immunising agent.

Dose : By subcutaneous injection, 1 ml (first dose); 1 ml (second dose) after an interval of seven to ten days. A single dose of 3 ml may be given in the event of an emergency.

Standards : Plague Vaccine is a sterile suspension of killed plague bacilli (*Yersinia pestis*) of the 195/p strain grown in a suitable enriched medium such as acid hydrolysate of casein, harvested and killed by the addition of formaldehyde. It may contain a suitable preservative. It has a median effective immunising dose (ED_{50}) for mouse of 0.004 ml or less.

Description : Turbid, whitish liquid free from flakes or clumps; nearly odourless or with a faint odour of the preservative.

Sterility : Complies with the *test for sterility*, Appendix 4.6.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Undue toxicity : Complies with the *test for undue toxicity for vaccines and sera*, Appendix 2.37.

Potency : Carry out the *biological assay of plague vaccine*, Appendix 2.23.

Storage : Store at a temperature between 2° and 8° The vaccine must not be frozen.

Labelling : The label on the container states (1) the storage conditions; (2) the date after which the contents are not intended to be used; (3) "Not to be frozen"

Human Plasma

Normal Human Plasma

Category : Plasma volume restorer.

Description : Slightly opalescent liquid of a faint yellow or amber colour; practically odourless. It contains no visible particles. On standing, the opalescence may increase or a precipitate of fibrin may develop.

Standards : Human Plasma is the fluid portion of Whole Human Blood, intended for intravenous use which has been collected, stabilised against clotting and separated from the red blood cells.

It may be prepared by pooling approximately equal amounts of the liquid portion of unclotted Whole Human Blood from several healthy donors not exceeding twelve in number. To ensure cross-neutralisation of haemagglutinins by soluble blood group substances, the supernatant fluids are pooled so that contributions from donors of A, O and either B or AB groups are represented in approximately the ratio 9:9:2. The blood from each donor is withdrawn under aseptic conditions into individual sterile containers containing suitable anticoagulant solutions and the cell-free plasma is separated either by centrifuging or sedimentation of the red cells. The clear supernatant plasma is removed in a closed system under aseptic conditions and then pooled. The following conditions have to be satisfied before the individual tests of plasma are considered suitable for pooling:

(a) No blood will be used which shows visible evidence of haemolysis or of any bacterial contamination.

(b) No blood will be used which has been stored at a temperature exceeding 10° for a period more than five hours or has been exposed to a temperature higher than 25°.

(c) The cell-free plasma is collected from Whole Human Blood which has been stored at a temperature between 1° and 6°, within four weeks of collection.

The pooled plasma is distributed into the final containers aseptically and stored at a temperature of 1° to 6° within four hours after filling. Tests for sterility are done at each stage of processing.

It contains not less than 4.5 per cent w/v of protein.

Identification : (A) Precipitation tests with specific antisera show that the preparation consists only of plasma proteins of human origin.

(B) To 1 ml add 0.2 ml of a 2.5 per cent w/v solution of *calcium chloride*; coagulation occurs, which can be accelerated by heating at 37°.

Haemoglobin : Not more than 0.025 per cent w/v, determined by the following method: To 0.5 ml in a glass-stoppered test-tube add 2.0 ml of a reagent consisting of 9 ml of *pyridine*, 1 g of *resorcinol*, 5 g of *aminophenazone* and sufficient *alcohol* to produce 100 ml. Add 1.0 ml of a mixture of 8 volumes of *glacial acetic acid* and 92 volumes of *alcohol* and 1.0 ml of dilute hydrogen peroxide solution (0.6 per cent w/v H_2O_2), close the tube, mix the contents by inversion and keep aside for 45 minutes. Dilute with an equal volume of *water* and filter. Measure the *extinction* of a 1-cm layer of the resulting solution at 500 nm, Appendix 5.15 A, using as the blank 0.5 ml of the substance being examined, treated in a similar manner but replacing the hydrogen peroxide solution by *water*. Calculate the haemoglobin content from the *extinction* obtained by carrying out the test on a solution of haemoglobin of known concentration as determined by its iron content, calculated from the formula:

$$\text{Hemoglobin content (g/litre)} = \frac{\text{Iron content (mg/litre)}}{0.303}$$

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using 3 ml per kg of the rabbit's weight and rabbits that have not previously received blood products.

Sterility : Complies with the *tests for sterility*, Appendix 4.6.

Assay : To 2.0 ml in a round-bottomed centrifuge tube add 5 ml of *water* mix, add 0.2 ml of a 7.5 per cent w/v solution of *sodium molybdate* and 2 ml of a mixture consisting of 1 volume of *nitrogen-free sulphuric acid* and 30 volumes of *water*. Shake, centrifuge for five minutes, decant the supernatant liquid and allow the inverted tube to drain on filter paper. To the residue in the tube, add three drops of a 30 per cent w/v solution of *copper sulphate* and 1 ml of *nitrogen-free sulphuric acid* and boil gently for ten minutes; cool, add 1 g of *anhydrous sodium sulphate*

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

and 10 mg of *selenium*, boil gently for one hour and cool. Transfer to an ammonia distillation apparatus, add 6 ml of a saturated solution of *sodium hydroxide* and pass steam through the flask; distil for seven minutes, collecting the distillate in a mixture of 5 ml of a saturated solution of *boric acid*, 5 ml of *water*, and 1 drop of a saturated solution of *methyl red* in *alcohol* containing 0.1 per cent of *methylene blue*, and titrate with *0.02N hydrochloric acid*. Each ml of *0.02N hydrochloric acid* is equivalent to 0.00175 g of protein.

Storage : Store in sterile containers sealed so as to exclude micro-organisms, at a temperature between 1° and 6°. Protect from light.

Labelling : The label on the container states (1) the name and percentage of anticoagulant used; (2) the number of donors from whom the contents have been derived; (3) the protein content; (4) the storage conditions; (5) the date after which the preparation is not intended to be used for transfusion.

Dried Human Plasma

Category : Plasma volume restorer.

Description : Pale to deep cream-coloured powder or friable egglomerate.

Standards : Dried Human Plasma is prepared from a pool of Normal Human Plasma by freeze-drying or by any other method which will avoid denaturation of the proteins and will yield a product readily soluble in a quantity of *water* equal to the volume of the liquid from which the substance was prepared. It contains no preservative. The pooled plasma is distributed into its final sterile containers, dried and the containers sealed so as to exclude air, moisture and microbial contamination.

When reconstituted with the volume of Water for Injection, stated on the label, the solution contains not less than 4.5 per cent w/v of protein.

Solubility : Add a volume of *water* at 20° indicated on the label to the contents of a sealed container and shake gently, avoiding frothing; the substance dissolves completely within ten minutes to give a yellow liquid, free from visible particles and signs of haemolysis.

Loss on drying : Not more than 0.5 per cent, determined on 2.0 g by drying "in vacuo" for 24 hours, Appendix 5.8.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using 3 ml of the reconstituted plasma per kg of the rabbit's weight, and rabbits that have not previously received blood products.

Sterility : Complies with the *tests for sterility*, Appendix 4.6.

Reconstitute the contents of the sealed container with the requisite amount of *water for injection*. The reconstituted solution complies with the tests for **Identification, Haemoglobin and Assay**, described under Normal Human Plasma.

Storage : Store in an atmosphere of nitrogen in sterile, light-resistant containers sealed so as to exclude micro-organisms, in a cool place.

Labelling : The label on the container states (1) the name and percentage of anticoagulant used; (2) the volume of plasma when reconstituted; (3) the volume of Water for Injection to be added; (4) the number of donors from whom the contents were derived; (5) that the reconstituted solution must be used immediately; (6) the storage conditions; (7) the date after which the preparation is not intended to be used for transfusion.

Human Plasma Protein Fraction

Human Albumin Fraction (Saline)

Category : Blood volume supporter.

Dose : By intravenous infusion, 250 to 500 ml.

Description : Transparent, nearly colourless or slightly brownish liquid; almost odourless. On storage, a slight, granular or flaky deposit may develop.

Standards : Human Plasma Protein Fraction is a sterile solution of protein composed of albumin and globulin, derived from human blood. It exerts a colloid osmotic pressure approximately equivalent to that of pooled liquid human plasma containing 5.2 per cent w/v of protein; it contains no fibrinogen or antibodies. It is obtained from liquid human blood, plasma or serum from healthy human donors, determined at the time of donation to have been free from disease-causative agents that are not destroyed or removed by the processing method, as determined by medical history of the donor and from such physical examination and clinical tests as may be necessary at the time the blood was obtained. It may be prepared by precipitation with suitable organic solvents under controlled conditions of pH, ionic strength and temperature or by any other method which shall not affect the integrity of the product and shall have been shown to yield consistently a product which is safe for intravenous injection. Residual solvent, if present, is

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

removed by freeze-drying or other suitable treatment. The product is dissolved in water and sufficient quantities of suitable substances are added to stabilise it to heat, and Sodium Chloride to adjust the sodium ions to between 130 and 160 millimoles per litre. No bactericide or antibiotic is added at any stage during preparation. The solution is sterilised by filtration, distributed aseptically into containers, and then sealed so as to exclude micro-organisms. It is then heated to, and maintained for ten hours at 59.5° to 60.5° so as to prevent the transmission of serum hepatitis. Finally, the containers are incubated for not less than 14 days at 30° to 32° and examined visually. Those showing abnormalities such as abnormal colour, turbidity, microbial contamination, or presence of atypical particles shall be discarded.

Human Plasma Protein Fraction contains not less than 4.3 per cent and not more than 5.5 per cent w/v of total protein and not more than 2 millimoles of potassium ions per litre.

Identification : (A) By precipitation tests with specific antisera, contains plasma proteins of human origin only

(B) By *electrophoresis*, using the moving boundary technique in *barbitone buffer solution, pH 8.6* and ionic strength 0.1, has not less than 83 per cent of the protein having the mobility of albumin, and not more than 17 per cent of globulins. Not more than 1 per cent of the total proteins shall be gamma globulin, Appendix 5.9.

pH : Between 6.7 and 7.3, Appendix 5.10.

Denatured protein : Complies with the test described under Normal Human Serum Albumin, except that the weight of protein in the fraction of the eluate is not more than 5 per cent of the weight of protein in the volume of the substance being examined applied to the column.

Haem content; Stability; Pyrogens; Sterility; Undue toxicity and Assay : Complies with the tests described under Normal Human Serum Albumin.

Storage : Store at a temperature between 2° and 25° and protect from light.

Labelling : The label on the container states (1) the volume; (2) the total amount of protein; (3) the concentration of sodium and potassium ions; (4) the name and concentration of any stabilising agents added; (5) the type of source material used to manufacture the product; (6) the words "do not use if turbid or more than 4 hours after the container has been entered"; (7) the storage conditions; (8) the date after which the solution is not intended to be used.

Plaster of Paris

Dried Calcium Sulphate

$CaSO_4, \frac{1}{2}H_2O$ Mol. Wt. 145.15

Category : Surgical aid.

Description : White hygroscopic powder; odourless or almost odourless; tasteless.

Solubility : Slightly soluble in *water*, solubility decreasing sharply with rise of temperature; more soluble in dilute mineral acids; practically insoluble in *alcohol*.

Standards : Dried Calcium Sulphate is prepared by heating powdered gypsum, $CaSO_4, 2H_2O$, at about 150° until three quarters of the water of crystallisation is lost.

Identification : (A) It gives the reactions of *calcium*, and of *sulphates*, Appendix 3.1.

pH : Between 6.5 and 9.0, determined in a 20 per cent w/v slurry in *water*, Appendix 5.10.

Acid insoluble matter : Dissolve 0.5 g in 30 ml of a mixture of 1 volume of *hydrochloric acid* and 2 volumes of *water* and evaporate to dryness in a dish on a water-bath. Heat for two hours at 120° and again add 20 ml of the acid mixture. Warm for a few minutes and filter. Wash the residue with warm *water* to free it from chlorides, dry, ignite, and weigh. The residue weighs not more than 5 mg.

Setting properties : 20 g mixed with 10 ml of *water* at 15° to 20° in a cylindrical mould about 2.4 cm in diameter sets in not less four minutes and not more than six minutes. The mass thus formed, after standing for three hours, possesses sufficient hardness to resist pressure of the fingers at the edges, which retain their sharpness of outline and do not crumble under pressure.

Loss on ignition : Between 6.0 and 9.0 per cent, determined by igniting to constant weight at red heat.

Storage : Store in tightly-closed containers.

Poliomyelitis Vaccine (Oral)

Poliomyelitis Vaccine (Live; Poliovirus Vaccine Live Oral)

Category : Active immunising agent.

Dose : The dose of each type of monovalent vaccine, six to eight weeks apart and a fourth, reinforcing dose of the trivalent vaccine, eight to twelve months later.

Description : Clear liquid which may have a red-

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

dish colour if phenol red has been used in its preparation.

Standards : Poliomyelitis Vaccine (Oral) is an aqueous suspension of one or a combination of the two or three types of live attenuated strains of poliomyelitis virus, tested for neurovirulence in monkeys in comparison with the Standard Attenuated Poliomyelitis Virus Type 1 and for immunogenicity and found to be suitable for human immunization in adequate clinical trials.

The final vaccine represents not more than three subcultures of types 1 and 2 and not more than two subcultures of type 3 from the vaccine on which tests for suitability were done. The virus of each type is grown, with aseptic precautions, in cultures of suitable tissue, free from extraneous micro-organisms, and adventitious agents. The medium for maintaining cell growth, as distinct from that for initiating it, contains no serum but may contain a suitable pH indicator such as phenol red. Suitable antibiotic in small concentrations may be used but penicillin and streptomycin may not be used. The medium is maintained at a temperature not exceeding 35° during the growth of the virus.

The harvesting of the virus is done within four days of inoculation and the virus suspension is tested for identity, sterility and freedom from adventitious viral agents. Harvests which pass these tests are pooled and filtered through a bacteria-proof filter.

NOTE – The manufacturing method or process or the conditions under which it is conducted as given in the above Standards may be modified provided the manufacturer presents to the Licencing Authority under the Drugs & Cosmatics Rules, 1945, evidence to show that the modification will provide assurance of the Safety, Purity and Potency of the vaccine that are equal to or greater than the assurance provided by these standards. The filtered virus harvest is tested for identity and virus concentration. The polio virus in the filtered bulk suspension is also tested in comparison with appropriate reference virus preparation for: (a) neurovirulence in suitable species of monkeys by intraspinal inoculation and statistical evaluation of the severity of local reaction and the degree of its spread in the CNS, (b) the reproductive capacity at supraoptimal temperature of 40°C (RCT_{40}) by growing the virus at two temperatures of 36°C and 39°C to 41°C to show that the vaccine virus strain does not multiply at elevated temperatures. The final vaccine is constituted by combining appropriate dilutions of the three virus types and by the addition of approved additives.

Identification : When neutralised with appropriate specific poliomyelitis aniserum, it is unable to infect susceptible tissue cultures.

Freedom from adventitious viral agents : When neutralised with type-specific poliomyelitis antiserum or antisera, the neutralised mixture, when inoculated into susceptible tissue cultures does not show the presence of adventitious viral agents.

Sterility : Complies with the *tests for sterility*, Appendix 4.6.

Undue toxicity : Complies with the *test for undue toxicity for vaccines and sera*, Appendix 2.37.

NOTE – That test may not be performed if magnesium chloride is used as a stabiliser.

Virus concentration : Titrate for live virus, using five tubes of cell cultures for each 0.5 $\log_{10}$ dilution or by any other method of equal sensitivity. The estimated virus titre is not less than the declared titre and in any case shall be in the range of 6.0 ± 0.3 $\log_{10}$ $TCID_{50}$ for type 1, 5.48 ± 0.3 $\log_{10}$ $TCID_{50}$* for type 3, and 5.0 ± 0.3 $\log_{10}$ $TCID_{50}$ for type 2 per one human oral dose. The total virus concentration, thus shall be within the range of 6.14 ± 0.3 $\log_{10}$ $TCID_{50}$ per one human dose.

Storage : Store in single-dose or multiple-dose containers in the frozen state at −28° or below. When thawed it should be kept at a temperature of 0° to 40° and used within three months. If stored at a temperature between 18° and 20° it should be used within a few hours.

Labelling : The label on the container states (1) the type or types of poliomyelitis virus; (2) the virus concentration; (3) the recommended dose and number of doses in the container; (4) that the vaccine is for oral administration only; (5) the name and proportion of any added preservative or stabiliser; (6) the storage conditions; (7) the date after which it is not intended to be used.

Polyethylene Glycol 1500

Category : Pharmaceutical aid (ointment base).

Description : White or almost white, soft, wax-like solid; odour, faint and characteristic.

Solubility : Freely soluble in *water*, and in *chloroform*; sparingly soluble in *ethyl alcohol*; insoluble in *solvent ether*.

Standards : Polyethylene Glycol 1500 is a polymer of ethylene oxide and water, represented by the

* The statistically determined quantity of virus which infects 50 per cent of the cell cultures to which it is added.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

formula $H(OCH_2CH_2)n\,OH$ in which the average value of n is between 28 and 36.

Congealing range : Between 42° and 48°, Appendix 5.5.

pH : Between 4.0 and 7.5, determined in a 5.0 per cent w/v solution, Appendix 5.10.

Viscosity : Between 25 cs and 32 cs, determined at 100°, Appendix 5.18.

Hydroxyl value : Between 70 and 86, Appendix 3.3.17.

Arsenic : Not more than 3 parts per million, Appendix 3.2.1.

Heavy metals : Not more than 5 parts per million, determined by Method A on a solution of 4 g in 5.0 ml of a 1.0 per cent w/v solution of *hydrochloric acid* and sufficient *water* to produce 25 ml, Appendix 3.2.4.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Storage : Store in tightly-closed containers.

Polyethylene Glycol 4000

Category : Pharmaceutical aid (ointment base and tablet excipient).

Description : Creamy-white, hard, wax-like solid, powder or flakes; odour, faint and characteristic.

Solubility : Freely soluble in *water*; in *alcohol* and in *chloroform*; insoluble in *solvent ether*.

Standards : Polyethylene Glycol 4000 is a polymer of ethylene oxide and water, represented by the formula $H(OCH_2 \cdot CH_2)n\,OH$, in which the average value of n is between 68 and 84.

Congealing range : Between 54° and 58°, Appendix 5.5.

Clarity and colour of solution : A 10.0 per cent w/v solution is practically clear and colourless.

Viscosity : Between 76 cs and 110 cs, determined at 100°, Appendix 5.18.

Hydroxyl value : Between 30 and 36, Appendix 3.3.17.

pH; Arsenic; Heavy metals and Sulphated ash : Complies with the requirements stated under Polyethylene Glycol 1500.

Storage : Store in tightly-closed containers.

Polyethylene Glycol 6000

Category : Pharmaceutical aid (ointment base and tablet excipient).

Description : White to creamy-white waxy solid or flakes; odour, faint and characteristic.

Solubility : Freely soluble in *water*, in *alcohol*, and in *chloroform*; insoluble in *solvent ether*.

Standards : Polyethylene Glycol 6000 is a polymer of ethylene oxide and water, represented by the formula $H(OCH_2.CH_2)nOH$, in which the average value of n is between 158 and 204. It has an average weight of not less than 7000 and not more than 9000.

Congealing range : Between 56° and 63°, Appendix 5.5.

Viscosity : Between 470 cs and 900 cs, determined at 100°, Appendix 5.18.

pH : Between 4.5 and 7.5, determined in a 5.0 per cent w/v solution, Appendix 5.10.

Arsenic; Heavy metals and Sulphated ash : Complies with the requirements stated under Polyethylene Glycol 1500.

Average molecular weight : *Phthalic anhydride-Pyridine solution*—Weigh accurately 42 g of *phthalic anhydride* and add to 300 ml of freshly distilled *pyridine* (refluxed with barium oxide) containing less than 0.1 per cent of water, in a glass-stoppered, light resistant flask. Shake vigorously until complete solution is effected and allow to stand overnight to complete the reaction.
Method—Melt a sample in a water-bath maintained at 80°. Weigh accurately about 50 g of the melted sample and transfer to a 100-ml volumetric flask and dilute to volume with *pyridine*. Transfer to a pressure flask 25.0 ml of this solution and add 25.0 ml of *phthalic anhydride-pyridine solution*. Insert the stopper in the flask, wrap it securely with a piece of cloth, and immerse in a water-bath maintained at about 100° to the same depth as the mixture in the flask, for one hour. Remove the flask, retaining the cloth wrapping, and allow to cool in air to room temperature. Add 50.0 ml of *0.5N sodium hydroxide* and five drops of a 1 per cent w/v solution of *phenolphthalein* in *pyridine*. Titrate with *0.5N sodium hydroxide* to a pink end-point which is stable for not less than fifteen seconds. Perform a blank determination. Calculate the average molecular weight by multiplying the weight, in g of sample taken by 4000 and dividing the result by the difference between the volume, in ml, of *0.5N sodium hydroxide* consumed in the sample titration and the blank titration.

Storage : Store in tightly-closed containers.

Polysorbate 20

Category : Pharmaceutical aid (surfactant).

Description : Yellow to amber-coloured, oily, clear

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

liquid; odour, faint and characteristic; taste, somewhat bitter.

Solubility : Very soluble in *water*, producing an odourless and almost colourless solution; soluble in *alcohol*, in *methyl alcohol*, in *ethyl acetate* and in *dioxan*; practically insoluble in fixed oils and in *liquid paraffin*.

Standards : Polysorbate 20 is a mixture of partial lauric esters of sorbitol and it's anhydrides copolymerised with approximately 20 moles of ethylene oxide for each mole of sorbitol and sorbitol anhydrides.

Identification : (A) Dissolve 0.5 g in *water* at about 50° and dilute to 10 ml with *water*. The solution produces considerable foam on shaking. Add 0.5 g of *sodium chloride* and heat the solution to boiling. The resulting cloudiness disappears during cooling to about 50°

(B) To 2 ml of a 5 per cent w/v solution add 10 ml of *ammonium cobaltothiocyanate solution* and 5 ml of *chloroform*, shake well, and allow to separate; a blue colour is produced in the chloroform layer.

Specific gravity : Between 1.05 and 1.15, Appendix 5.19.

pH : Between 5.0 and 7.0, determined in a 5.0 per cent w/v solution; in *carbon dioxide-free water*, Appendix 5.10.

Acid value : Not more than 2.0, determined on 5.0 g dissolved in 50 ml of a mixture of equal volumes of *alcohol* and *solvent ether*, Appendix 3.3.15.

Iodine value : Not more than 5.0, Appendix 3.3.18.

Saponification value : Between 40 and 50, using 15.0 ml of *0.5N alcoholic potassium hydroxide* and diluting with 50 ml of *water* before carrying out the titration, Appendix 3.3.20.

Viscosity : Between 240 cs and 350 cs at 25°, Appendix 5.18.

Arsenic : Not more than 1 part per million, Appendix 3.2.1.

Heavy metals : Not more than 10 parts per million, determined on 2.0 g by Method B, Appendix 3.2.4.

Reducing impurities : Dissolve 2 g in 25 ml of hot *water*, add 25 ml of *dilute sulphuric acid*, and two drops of *ferroin sulphate solution*; titrate with *0.01N ceric ammonium sulphate* to a greenish-blue end-point which persists for 30 seconds. Carry out a blank test. Not more than 2.0 ml of *0.01N ceric ammonium sulphate* is required.

Sulphated ash : Not more than 0.2 per cent, Appendix 3.2.7.

Water : Not more than 3.0 per cent w/w, Appendix 3.3.25.

Storage : Store in tightly-closed containers.

Polysorbate 80

Category : Pharmaceutical aid (surfactant).

Description : Yellow to amber-coloured, oily, clear liquid; odour, faint and characteristic; taste, slightly bitter.

Solubility : Very soluble in *water*, producing an odourless and almost colourless solution; soluble in *alcohol*, in *ethyl acetate* and in vegetable oils; insoluble in fixed oils and in *liquid paraffin*.

Standards : Polysorbate 80 is a mixture of partial oleic esters of sorbitol and its anhydrides copolymerised with approximately 20 moles of ethylene oxide for each mole of sorbitol and sorbitol anhydrides.

Identification : (A) To 5 ml of a 5 per cent w/v solution add 5 ml of *N sodium hydroxide* and boil for a few minutes. Cool, and acidify with *dilute hydrochloric acid*; an opalescent solution is produced.

(B) To 5 ml of a 5 per cent w/v solution add 1 ml of *bromine water*; the bromine is decolorised.

(C) To 6 ml add 4 ml of *water*; a gelatinous mass is produced at normal and lower than normal room temperatures.

Specific gravity : Between 1.07 and 1.09, Appendix 5.19.

pH : Between 6.0 and 8.0, determined in a 5.0 per cent w/v solution in *carbon dioxide-free water*, Appendix 5.10.

Acid value : Not more than 2.0, determined on 5.0 g dissolved in 5.0 ml of mixture of equal volumes of *alcohol* and *solvent ether*, Appendix 3.3.15.

Iodine value : Between 18 and 24, Appendix 3.3.18.

Saponification value : Between 45 and 55, using 15.0 ml of *0.5N alcoholic potassium hydroxide* and diluting with 50 ml of *water* before carrying out the titration, Appendix 3.3.20.

Viscosity : Between 340 cs and 450 cs at 25°, Appendix 5.18.

Arsenic : Not more than 1 part per million, Appendix 3.2.1.

Heavy metals : Not more than 10 parts per million, determined on 2.0 g by Method B, Appendix 3.2.4.

Reducing impurities : Dissolve 2 g in 25 ml of hot *water*, add 25 ml of *dilute sulphuric acid*, and two drops of *ferroin sulphate solution*; titrate with *0.01N ceric ammonium sulphate* to a greenish-blue end-point which persists for 30 seconds. Carry out a blank test. Not more than 5.0 ml of *0.01N ceric ammonium sulphate* is required.

Sulphated ash : Not more than 0.2 per cent, Appendix 3.2.7.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Water : Not more than 3.0 per cent w/v, Appendix 3.3.25.

Storage : Store in tightly-closed containers.

Polyvinylpyrrolidone

Povidone

$(C_6H_9NO)x$

Category : Pharmaceutical aid (tablet binder and coating agent).

Description : White to creamy-white powder; odourless or almost odourless; hygroscopic.

Solubility : Soluble in *water*, in *alcohol* and in *chloroform*; insoluble in *solvent ether*.

Standards : Polyvinylpyrrolidone is a synthetic polymer consisting essentially of linear 1-vinyl-2-pyrrolidone groups, the degree of polymerisation of which results in polymers of various molecular weights. Commercial products are mixtures of polymers, each product having a particular mean molecular weight, in the range 10,000 to 700,000. Polyvinylpyrrolidone contains not less than 12.0 per cent and not more than 13.0 per cent of nitrogen, calculated with reference to the anhydrous substance.

Identification : (A) To 10 ml of a 2 per cent w/v solution add 20 ml of *N hydrochloric acid* and 5 ml of *potassium dichromate solution*; an orange-yellow precipitate is formed.

(B) Add 5 ml of a 2 per cent w/v solution to 2 ml of *ammonium cobaltothiocyanate solution* which has been acidified with *5N hydrochloric acid*; a pale-blue precipitate is formed.

(C) To 5 ml of a 0.5 per cent w/v solution add 0.2 ml of *0.1N iodine*; a deep red colour is produced.

pH : Between 3.0 and 7.0, determined in a 5.0 per cent w/v solution, Appendix 5.10.

Arsenic : Not more than 2 parts per million, Appendix 3.2.1.

Lead : Not more than 10 parts per million, determined by Method A on 1.0 g dissolved in 25 ml of *water*, Appendix 3.2.6.

Aldehydes : Not more than 0.5 per cent, calculated as $CH_3 \cdot CHO$ and determined by the following method: Add 10 g to 180 ml of *sulphuric acid (25 per cent v/v)* in a round-bottom flask, and attach the flask to a reflux condenser, the top of which is connected by means of an inverted U-shaped adaptor to the top of another vertical condenser at the lower end of which is attached a receiver, cooled in ice and containing 20 ml of *N hydroxylamine hydrochloride*. Heat the solution in the flask under reflux for forty-five minutes, discontinue the water supply to the reflux condenser, distil until about 100 ml of distillate is collected in the receiver, and titrate the contents of the receiver with *0.1N sodium hydroxide*, using *bromophenol blue solution* as indicator. Carry out a blank determination; the difference between the two titrations represent the amount of *0.1N sodium hydroxide* equivalent to the aldehydes present. Each ml of *0.1N sodium hydroxide* is equivalent to 0.004405 g of $CH_3 \cdot CHO$

Vinylpyrrolidone : Not more than 1.0 per cent, calculated as C_6H_9NO and determined by the following method: Weigh accurately about 4 g and dissolve in 30 ml of *water*, add 0.5 g of *sodium acetate*, and titrate with *0.1N iodine* until the colour due to iodine no longer fades: add a further 3 ml of *0.1N iodine*, allow to stand for ten minutes, and titrate the excess iodine with *0.1N sodium thiosulphate*, using *starch solution* as indicator. Each ml of *0.1N iodine* is equivalent to 0.005557 g of C_6H_9NO.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Water : Not more than 5.0 per cent w/w, Appendix 3.3.25.

Nitrogen content : Proceed as directed under *determination of nitrogen, Method A*, using 0.3 g accurately weighed, and 11 ml of *nitrogen-free sulphuric acid*, Appendix 3.3.5.

Storage : Store in tightly-closed containers.

Labelling : The label on the container states "Not suitable for preparing injections"

Potassium Bromide

KBr Mol. Wt. 119.00

Category : Sedative; anticonvulsant.

Dose : 0.3 to 1.2 g.

Description : Colourless crystals or white crystalline powder; odourless; taste, saline and slightly bitter.

Solubility : Freely soluble in *water* and in *glycerin*, slightly soluble in *alcohol*.

Standards : Potassium Bromide contains not less than 98.0 per cent of KBr, calculated with reference to the dried substance.

Identification : A solution (1 in 20) gives the reactions of *potassium*, and of *bromides*, Appendix 3.1.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Acidity or Alkalinity : 1.0 g dissolved in 10 ml of freshly boiled and cooled *water*, requires not more than 0.5 ml of *0.01N sodium hydroxide* or *0.01N hydrochloric acid* for neutralisation to *bromothymol blue solution*.

Clarity and colour of solution : A 10 per cent w/v solution is clear and colourless.

Bromates : To 10 ml of a 10 per cent w/v solution add 1 ml of *dilute sulphuric acid*, 1 ml of *chloroform* and shake thoroughly. The chloroform layer remains colourless.

Iodides : To 5 ml of a 10 per cent w/v solution add two or three drops of *ferric chloride solution*, heat for one minute on a water-bath, cool and shake with 2 ml of *chloroform*. The chloroform layer remains colourless.

Heavy metals : Not more than 10 parts per million, determined by Method A on 2 g dissolved in 10 ml of *water*, to which are added 2 ml of *dilute acetic acid* and 13 ml of *water*, Appendix 3.2.4.

Arsenic : Not more than 2 parts per million, Appendix 3.2.1.

Barium : To 5 ml of a 10.0 per cent w/v solution add 5 ml of *water* and 1 ml of *2N sulphuric acid*; the solution, after not less than fifteen minutes, is not more opalescent than a mixture of 5 ml of the 10.0 per cent solution and 6 ml of *water*.

Iron : 0.5 g complies with the *limit test for iron*, Appendix 3.2.5.

Sulphate : 2.0 g complies with the *limit test for sulphates*, Appendix 3.2.8.

Chlorides : Not more than the equivalent of 1.0 per cent, calculated as KCl and determined by the following method: To the solution obtained in the **Assay**, after titration with potassium permanganate, add one drop of *ammonium oxalate solution*, 5.0 ml of *0.1N silver nitrate* and 1 ml of *nitrobenzene*, shake, and add 2 ml of *ferric ammonium sulphate solution*. Titrate the solution with *0.1N ammonium thiocyanate* until a reddish-yellow colour is obtained. Each ml of *0.1N silver nitrate* is equivalent to 0.00746 g of KCl.

Sodium : Dissolve 0.3 g in 3.5 ml of *water*, add 2.0 ml of *alcohol*, and 1.0 ml of *potassium antimonate solution*, and allow to stand. No precipitate is formed within fifteen minutes.

Calcium and magnesium : Dissolve 1 g in 20 ml of *water*, add 1 ml of *dilute ammonia solution* and 1 ml of *sodium phosphate solution*; the solution remains clear.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 1.2 g, dissolve in *water* and dilute to 100.0 ml with *water*. To 10.0 ml of the solution, add 100 ml of *water*, 10 ml of *sulphuric acid* and a few glass beads. Heat to boiling and, while the solution is still boiling, titrate with *0.1N potassium permanganate* added dropwise until the pink colour just persists. Each ml of *0.1N potassium permanganate* is equivalent to 0.01190 g of KBr.

Storage : Store in well-closed containers.

Potassium Chloride

KCl Mol. Wt. 74.55

Category : Electrolyte replenisher.

Dose : 1 to 2 g.

Description : Colourless crystals or white crystalline powder; odourless; taste, saline.

Solubility : Freely soluble in *water*, practically insoluble in *alcohol* and in *solvent ether*.

Standards : Potassium Chloride contains not less than 99.0 per cent of KCl, calculated with reference to the dried substance.

Identification : A solution (1 in 20) gives the reactions of *potassium*, and of *chlorides*, Appendix 3.1.

Acidity or Alkalinity : 5.0 g dissolved in 50 ml of freshly boiled and cooled *water* requires not more than 0.5 ml of *0.01N sodium hydroxide* or *0.01N hydrochloric acid* for neutralisation to *bromothymol blue solution*.

Clarity and colour of solution : A 10 per cent w/v solution is clear and colourless.

Bromides and iodides : Digest 2 g, finely powdered, for three hours with 25 ml of warm *alcohol*, cool and filter. Evaporate the filtrate to dryness; dissolve the residue in 5 ml of *water*, add 1 ml of *chloroform* and then, drop by drop, *chlorine solution* diluted with twice its volume of *water*; the chloroform does not acquire a violet, yellow or orange colour.

Heavy metals; Sodium; Calcium and Magnesium : Complies with the tests described under Potassium Bromide.

Arsenic : Not more than one part per million, Appendix 3.2.1.

Barium : Complies with the tests described under Potassium Bromide.

Iron : 1.0 g complies with the *limit test for iron*, Appendix 3.2.5.

Sulphate : 2.0 g complies with the *limit test for sulphates*, Appendix 3.2.8.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105° for 2 hours, Appendix 5.8.

Assay : Weigh accurately about 0.25 g, dissolve in 50 ml of *water* and titrate with *0.1N silver nitrate*, using *potas-*

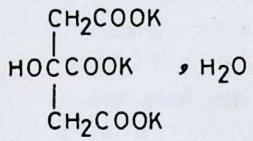
CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

sium chromate solution as indicator. Each ml of *0.1N silver nitrate* is equivalent to 0.007455 g of KCl.

Storage : Store in well-closed containers.

Potassium Citrate



$C_6H_5K_3O_7, H_2O$ Mol. Wt. 324.42

Category : Systemic alkaliser.

Dose : 4 to 10 g.

Description : White granular crystals, or crystalline powder; odourless; taste, saline. Slightly hygroscopic.

Solubility : Very soluble in *water*; practically insoluble in *alcohol*; soluble in *glycerin*.

Standards : Potassium Citrate is the monohydrate of tripotassium 2-hydroxy propane-1,2,3-tricarboxylate. It contains not less the 99.0 per and not more than the equivalent of 101.0 per cent of $C_6H_5K_3O_7$, calculated with reference to the anhydrous substance.

Identification : A solution (1 in 20) gives the reactions of *potassium*, and of *citrates*, Appendix 3.1.

Acidity or Alkalinity : 2.0 g boiled with 25 ml of *water*, and cooled, requires not more than 0.5 ml of ether *0.1N sulphuric acid* or *0.1N sodium hydroxide* for neutralisation to *thymol blue solution*.

Arsenic : Not more than 2 parts per million, Appendix 3.2.1.

Heavy metals : Not more than 10 parts per million determined on 2.0 g by Method A, Appendix 3.2.4.

Sodium : To 10 ml of a 10.0 per cent w/v solution add 6 ml of *potassium antimonate solution*; after fifteen minutes, the solution is clear, or at most very slightly opalescent.

Chloride : 0.5 g dissolved in *water* with addition of 2 ml of *nitric acid*, complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphates : 0.5 g dissolved in water with addition of 2 ml of *hydrochloric acid*, complies with the *limit test for sulphates*, Appendix 3.2.8.

Oxalate : Dissolve 1 g in a mixture of 1.5 ml of *water* and 2.5 ml of *dilute hydrochloric acid*, add 4 ml of *alcohol* and 4 drops of *calcium chloride solution*, and allow to stand for one hour; the mixture remains clear.

Readily carbonisable substances : Heat 1.0 g, in powder, with 10 ml of *sulphuric acid* for thirty minutes on a water-bath at 80° to 90° for one hour; the solution is not more intensely coloured than a mixture of 1.44 ml of *ferric chloride C.S.*, 0.03 ml of *copper sulphate C.S.*, 0.03 ml of *cobalt chloride C.S.* and 8.5 ml of *hydrochloric acid (1 per cent w/v)*.

Water : Between 4.0 and 7.0 per cent w/w, determined on 0.50 g, Appendix 3.3.25. After stirring, allow the substance being examined to remain in contact with the *dehydrated methyl alcohol* for fifteen minutes, stir again for one minute, and then titrate.

Assay : Weigh accurately about 0.15 g, add 20 ml of *glacial acetic acid* and heat to about 50° to effect solution. Cool, add 0.25 ml of *1-naphtholbenzein solution* and titrate with *0.1N perchloric acid* until a green colour is obtained. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.01021 g of $C_6H_5K_3O_7$.

Storage : Store in well-closed containers.

Potassium Iodide

KI Mol. Wt. 166.00

Category : Antifungal; expectorant; source of iodine.

Dose : As expectorant, 250 to 500 mg. In pre-operative treatment of thyrotoxicosis, 30 to 60 mg.

Description : Colourless crystals or white powder; odourless; taste, saline and slightly bitter.

Solubility : Very soluble in *water* and in *glycerin*; soluble in *alcohol*.

Standards : Potassium Iodide contains not less than 99.0 per cent of KI, calculated with reference to the dried substance

Identification : A solution (1 in 20) gives the reactions of *potassium*, and of *iodides*, Appendix 3.1.

Alkalinity : Dissolve 1 g in 10 ml of freshly boiled and cooled *water*, and add 0.2 ml of *0.02N sulphuric acid*; no colour is produced on addition of a drop of *phenolphthalein solution*.

Arsenic : Not more than 2 parts per million, Appendix 3.2.1.

Heavy metals : Not more than 10 parts per million, determined on 2.0 g by Method A, Appendix 3.2.4.

Barium : Dissolve 0.5 g in 10 ml of *water* and add 1 ml of *dilute sulphuric acid*; no turbidity develops within one minute.

Cyanides : Dissolve 0.5 g in 5 ml of warm *water*, add one

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

drop of *ferrous sulphate solution* and 0.5 ml of *sodium hydroxide solution* and acidify with *hydrochloric acid*; no blue colour is produced.

Iodates : Dissolve 0.5 g in 10 ml of freshly boiled and cooled *water*, and add 2 drops of *dilute sulphuric acid* and a drop of *starch solution*; no blue colour is produced within two minutes.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g of previously powdered substance, by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.5 g, dissolve in about 10 ml of *water* and add 35 ml of *hydrochloric acid* and 5 ml of *chloroform*. Titrate with *0.05M potassium iodate* until the purple colour of iodine disappears from the chloroform. Add the last portion of the iodate solution dropwise and agitate vigorously and continuously. Allow to stand for five minutes. If any colour develops in the chloroform layer continue the titration. Each ml of *0.05M potassium iodate* is equivalent to 0.0166 mg of KI.

Storage : Store in well-closed containers.

Potassium Permanganate

$KMnO_4$ Mol.Wt. 158.03

Category : Anti-infective (topical).

Description : Dark purple, slender, prismatic crystals, having a metallic lustre; odourless; taste, sweet and astringent.

Solubility : Soluble in *water*; freely soluble in boiling *water*.

Standards : Potassium Permanganate contains not less than 99.0 per cent of $KMnO_4$.

Identification : (A) A solution in *water*, acidified with *sulphuric acid* and heated to 70°, is decolorised by *hydrogen peroxide solution*.

(B) Heated to redness, it decrepitates, evolves oxygen, and leaves a black residue which with *water* forms potassium hydroxide solution; the resulting solution when neutralised with *dilute hydrochloric acid*, gives the reactions of *potassium*, Appendix 3.1.

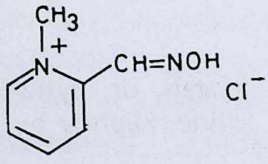
Chloride and sulphate : Dissolve 1 g in 50 ml of boiling *water*, heat on a water-bath, and add gradually 4 ml or a sufficient quantity of *alcohol* until the meniscus is colourless; filter. A 20 ml portion of the filtrate complies with the *limit test for chloride*, Appendix 3.2.2, and another 20 ml portion of the filtrate complies with the *limit test for sulphates*, Appendix 3.2.8.

Assay : Weigh accurately about 0.8 g, dissolve in *water* and dilute to 250 ml. Titrate with this solution 25.0 ml of *0.1N oxalic acid* mixed with 25 ml of *water* and 5 ml of *sulphuric acid*. Keep the temperature at about 70° throughout the entire titration. Each ml of *0.1N oxalic acid* is equivalent to 0.00316 g of $KMnO_4$.

Storage : Store in well-closed containers.

CAUTION – Great care should be observed in handling potassium permanganate, as dangerous explosions are liable to occur if it is brought into contact with organic or other readily oxidisable substance, either in solution or in the dry condition.

Pralidoxime Chloride



$C_7H_9ClN_2O$ Mol. Wt. 172.61

Category : Antidote for cholinesterase inhibitors.

Dose : By intravenous injection – 1 to 2 g as a 5 per cent solution, over not less than a five-minute period.

Description : White to pale-yellow crystalline powder; odourless.

Solubility : Freely soluble in *water*, sparingly soluble in *alcohol*.

Standards : Pralidoxime Chloride is 2-Hydroxyiminomethyl-1-methylpyridinium chloride. It contains not less than 97. 0 per cent and not more than the equivalent of 103.0 per cent of $C_7H_9ClN_2O$, calculated with reference to the dried substance.

Identification : (A) The light absorption, in the range 240 to 350 nm of a 1-cm layer of a 0.0005 per cent w/v solution in *0.1N hydrochloric acid* exhibits maxima at 242 nm and 292 nm and in *0.1N sodium hydroxide*, a maximum at 332 nm, Appendix 5.15 A.

(B) To 2 drops of a 20 per cent w/v solution, add 1 ml of a 0.6 per cent w/v solution of *ferric chloride*; an amber-brown colour is produced.

(C) To 0.5 ml of *2N sodium hydroxide* add 1 ml of a 20 per cent w/v solution of the substance; a bright yellow colour is produced. The colour change is reversed on acidifying with *2N hydrochloric acid*.

(D) A solution (1 in 10) gives the reactions of *chlorides*, Appendix 3.1.

Melting range : Between 215° and 225° with decomposition, Appendix 5.11.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Heavy metals : Not more than 20 parts per million, determined on 1.0 g by Method A, Appendix 3.2.4.

Chloride content : Between 20.2 per cent and 20.8 per cent, calculated with reference to the dried substance, and determined by the following method: Weigh accurately about 0.3 g, dissolve in about 150 ml of *water*, add 20 ml of *glacial acetic acid* and 10 drops of *(p-tert-octylphenoxy) nonaethoxyethanol*, and titrate with *0.1 N silver nitrate*, determining the end-point potentiometrically. Each ml of *0.1 N silver nitrate* is equivalent to 0.003545 g of Cl.

Sulphated ash : Not more than 0.5 per cent, Appendix 3.2.7.

Loss on drying : Not more than 2.0 per cent, determined on 1.0 g by drying in an oven at 105° for three hours, Appendix 5.8.

Assay : Weigh accurately about 0.5 g and dissolve in sufficient *water* to produce 250.0 ml. Dilute 5.0 ml of this solution to 100.0 ml with *water*. Transfer 5.0 ml of the resulting solution to a 50-ml volumetric flask, dilute to about 40 ml with *water*, add 5.0 ml of *N sodium hydroxide* and dilute to volume with *water*. Within ten minutes of the addition of the alkali, measure the *extinction* of the solution at the maximum at about 336 nm, Appendix 5.15 A, using a solution of 5.0 ml of *N sodium hydroxide* diluted with *water* to 50.0 ml as the blank. Calculate the content of $C_7H_9ClN_2O$, from the *extinction* obtained by carrying out the assay simultaneously using about 0.5 g accurately weighed, of *pralidoxime chloride R.S.*, and from the declared content of $C\text{-}H_9ClN_2O$ in the *pralidoxime chloride R.S.*

Storage : Store in well-closed containers.

Pralidoxime Chloride Injection

Category : Antidote for cholinesterase inhibitors.

Dose : Pralidoxime Chloride. By intravenous injection, 1 to 2 g as a 5 per cent solution over not less than a five-minute period.

Usual strength : 1 g.

Description : White to pale-yellow crystalline powder.

Standards : Pralidoxime Chloride Injection is a sterile solution of Pralidoxime Chloride in Water for Injection. It may contain suitable buffering agents. It is prepared immediately before use by dissolving the contents of a sealed container in the requisite amount of Water for Injection under aseptic conditions. The sealed container contains not less than 92.5 per cent and not more than 110.0 per cent of the stated amount of Pralidoxime Chloride, $C\text{-}H_9ClN_2O$.

Uniformity of weight : Complies with the requirements for **Uniformity of weight**, stated under Injections.

Other requirements : Complies with the requirements stated under Injections.

The contents of the sealed container comply with the following requirements

Identification; Loss on drying and Heavy metals : Comply with the requirements described under Pralidoxime Chloride.

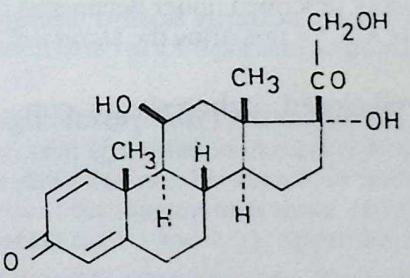
pH : Between 3.5 and 4.5 determined in a 5 per cent w/v solution, Appendix 5.10.

Pyrogens : Comply with the *test for pyrogens*, Appendix 2.36, using 25 mg per kg of the rabbit's weight, of a solution containing 25 mg per ml.

Assay : Carry out the **Assay** described under Pralidoxime Chloride.

Labelling : The label on the container states (1) the quantity of Pralidoxime Chloride in the container; (2) the storage conditions; (3) the date after which the contents are not to be used; (4) the period within which the prepared injection should be used.

Prednisolone



$C_{21}H_{28}O_5$ Mol. Wt. 360.45

Category : Adrenocortical steroid (anti-inflammatory).

Dose : 5 to 60 mg daily, in divided doses.

Description : White or almost white crystalline powder; odourless.

Solubility : Very slightly soluble in *water*; soluble in *alcohol*, in *methyl alcohol* and in *dioxan*; slightly soluble in *chloroform*; sparingly soluble in *acetone*.

Standards : Prednisolone is 11β, 17α, 21-trihydroxypregna-1,4-diene, 3, 20-dione. It contains not less than 96.0 per cent and not more than the equivalent

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

208/DGHS/ND/90—5,000 F-28

of 104.0 per cent of $C_{21}H_{28}O_5$, calculated with reference to the dried substance.

Identification : (A) Complies with the test for *identification of steroids*, Appendix 3.3.11, using *solvent I* and *mobile phase A* and applying to the plate 2 µl.

(B) Dissolve 10 mg in 1 ml of *methyl alcohol*, warm and add 1 ml of *potassium cupri-tartrate solution*; an orange red precipitate is slowly formed.

(C) Dissolve 2 mg in 2 ml of *sulphuric acid* and allow to stand for five minutes; an intense, red colour free form fluorescence is produced. Dilute the solution with 10 ml of *water*; the colour disappears and a grey flocculant precipitate is produced.

(D) It melts at about 230° with some decomposition, Appendix 5.11.

Specific optical rotation : Between +96° and +104°, determined in a 1.0 per cent w/v solution in *dioxan*, Appendix 5.12.

Light absorption : *Extinction* of a 1-cm layer of a 0.001 per cent w/v solution in *methyl alcohol* at the maximum at about 240 nm, between 0.40 and 0.43, Appendix 5.15 A; ratio of *extinction* at the maximum at about 240 nm to that at 263 nm is between 1.5 and 1.7.

Related foreign steroids : Complies with the test for *related foreign steroids, Method A*, Appendix 3.3.12.

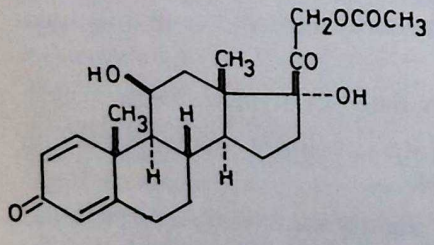
Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 0.5 g by drying in an oven at 105° for two hours, Appendix 5.8.

Assay : Carry out the **Assay** described under Betamethasone, using *prednisolone R.S.* for preparing the *standard solution.*

Storage : Store in well-closed, light-resistant containers.

Prednisolone Acetate



$C_{23}H_{30}O_6$ Mol. Wt. 402.49

Category : Adrenocortical steroid (anti-inflammatory).

Dose : 5 to 60 mg daily, in divided doses.

Description : White or almost white crystalline powder; odourless.

Solubility : Practically insoluble in *water*; slightly soluble in *alcohol*, and in *chloroform.*

Standards : Prednisolone Acetate is 11β, 17α, 21-trihydroxypregna-1,4-diene-3,20-dione 21-acetate. It contains not less than 96.0 per cent and not more than the equivalent of 104.0 per cent of $C_{23}H_{30}O_6$, calculated with reference to the dried substance.

Identification : (A) Complies with the test for *identification of steroids*, Appendix 3.3.11, using *solvent I* and *mobile phase B* and applying to the plate 2µl.

(B) Complies with the **Identification** tests (B) and (C) described under Prednisolone.

(C) To about 50 mg add 2 ml of *alcohol* and 2 ml of *sulphuric acid* and boil gently for about one minute; ethyl acetate recognisable by its odour, is evolved.

(D) It melts at about 235° with decomposition, Appendix 5.11.

Specific optical rotation : Between +112° and +119°, determined in a 1.0 per cent w/v solution in *dioxan*, Appendix 5.12.

Light absorption : *Extinction* of a 1-cm layer of a 0.0001 per cent w/v solution in *methyl alcohol* at the maximum at about 240 nm, between 0.355 and 0.385; ratio of *extinction* at the maximum at 240 nm to that at 263 nm, between 1.85 and 2.05, Appendix 5.15 A.

Related foreign steroids : Complies with the test for *related foreign steroids, Method A*, Appendix 3.3.12.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 0.5 g by drying in an oven at 105°, for two hours, Appendix 5.8.

Assay : Carry out the **Assay** described under Betamethasone, using *prednisolone acetate R.S.* for preparing the *standard solution.*

Storage : Store in well-closed, light-resistant containers.

Prednisolone Tablets

Category : Adrenocortical steroid (anti-inflammatory).

Dose : Prednisolone, 5 to 60 mg daily, in divided doses.

Usual strengths : 5 mg; 10 mg.

Standards : Prednisolone Tablets contain not less

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

208/DGHS/ND/90—3,000 F-28

than 90.0 per cent and not more than 110.0 per cent of the stated amount of Prednisolone, $C_{21}H_{28}O_5$.

Identification : (A) Shake a quantity of the powdered tablets equivalent to 15 mg of Prednisolone with 5 ml of *chloroform*, and evaporate the chloroform from the extract; the residue complies with **Identification** tests (A) and (B), described under Prednisolone.

(B) The residue obtained in **Identification** test (A) complies with the test for *related foreign steroids, Method A*, Appendix 3.3.12.

Uniformity of content : Powder one tablet, add 50 ml of *ethyl alcohol*, shake for thirty minutes and add sufficient *ethyl alcohol* to produce 100.0 ml. Centrifuge and pipette a suitable volume of the supernatant liquid equivalent to 0.5 mg of Prednisolone and dilute to 50.0 ml with *ethyl alcohol*. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 240 nm, Appendix 5.15 A. Calculate the content of $C_{21}H_{28}O_5$, taking 415 as the value of E(1 per cent, 1-cm) at the maximum at about 240 nm.

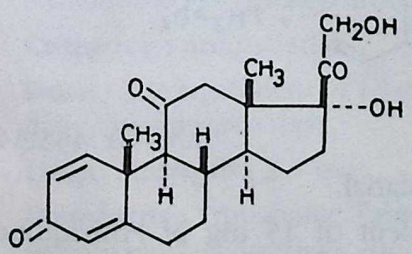
Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 90 and 110 per cent of the average except that for one tablet the content may be between 85 and 115 per cent of the average.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and finely powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 2.5 mg of Prednisolone, suspend in 10 ml of *water* and extract with 40, 20, 20 and 10 ml of *chloroform*. Wash each extract with the same 10 ml of *water*, filter, and dilute the combined filtrates to 250.0 ml with *chloroform*. Carefully evaporate 20.0 ml of the resulting solution to dryness and dissolve the residue in 20.0 ml of *aldehyde-free ethyl alcohol* to give the *test solution*. Carry out the *assay of steroids*, Appendix 3.3.10, using *prednisolone R.S.* for preparing the *standard solution*.

Storage : Store in well-closed, light-resistant containers.

Prednisone



$C_{21}H_{26}O_5$ Mol. Wt. 358.43

Category : Adrenocortical steroid (anti-inflammatory).

Dose : 5 to 60 mg daily, in divided doses.

Description : White or yellowish-white crystalline powder; odourless.

Solubility : Very slightly soluble in *water*; slightly soluble in *alcohol*, in *chloroform*, in *methyl alcohol*, and in *dioxan*.

Standards : Prednisone is 17α, 21-dihydroxypregna-1,4-diene-3,11,20-trione. It contains not less than 96.0 per cent and not more than the equivalent of 104.0 per cent of $C_{21}H_{26}O_5$, calculated with reference to the dried substance.

Identification : (A) Complies with the test for *identification of steroids*, Appendix 3.3.11, using *solvent I* and *mobile phase A* and applying to the plate 2 μl.

(B) Dissolve 6 mg in 2 ml of *sulphuric acid* and allow to stand for five minutes; an orange colour is produced. Pour the solution in 10 ml of *water*; the colour changes first to yellow and then gradually to bluish-green.

(C) Dissolve 0.2 mg in 1 ml of *alcohol*, evaporate to dryness under reduced pressure, add 5 ml of *N sodium hydroxide*, and heat at 70° for thirty minutes; not more than a slight yellow colour is produced (distinction from cortisone acetate).

(D) Complies with **Identification** test (B) described under Prednisolone.

(E) It melts at about 230° with decomposition, Appendix 5.11.

Specific optical rotation : Between +167° and +176°, determined in a 1.0 per cent solution in *dioxan*, Appendix 5.12.

Light absorption : *Extinction* of a 1-cm layer of a 0.001 per cent w/v solution in *methyl alcohol* at the maximum at about 240 nm, between 0.40 and 0.43; ratio of *extinction* at the maximum at about 240 nm to that at 263 nm, between 1.85 and 2.05, Appendix 5.15 A.

Related foreign steroids : Complies with the test for *related foreign steroids, Method A*, Appendix 3.3.12.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 0.5 g by drying in an oven at 105°. for two hours, Appendix 5.8.

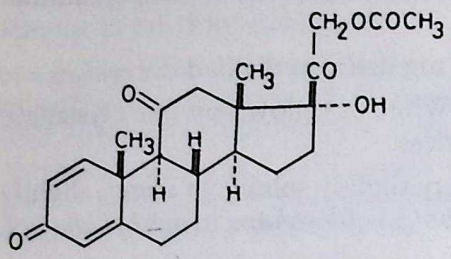
Assay : Carry out the **Assay** described under Betamethasone, using *prednisone R.S.* for preparing the *standard solution*.

Storage : Store in well-closed, light-resistant containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Prednisone Acetate



$C_{23}H_{28}O_6$ Mol. Wt. 400.47

Category : Adrenocortical steroid (anti-inflammatory).

Dose : 5 to 60 mg daily, in divided doses.

Description : White or almost white crystalline powder; odourless.

Solubility : Practically insoluble in *water*; slightly soluble in *alcohol*; freely soluble in *chloroform*.

Standards : Prednisone Acetate is 21-acetoxy-17 α, 21-dihydroxypregna-1,4-diene-3,11,20-trione 21-acetate. It contains not less than 96.0 per cent and not more than the equivalent of 104.0 per cent of $C_{23}H_{28}O_6$, calculated with reference to the dried substance.

Identification : (A) Complies with the test for *identification of steroids*, Appendix 3.3.11, using *solvent I* and *mobile phase B* and applying to the plate 2 µl.

(B) Complies with **Identification** test (C) described under Prednisone, with **Identification** test (B) described under Prednisolone, and with **Identification** test (C) described under Prednisolone Acetate.

(C) It melts at about 240° with decomposition, Appendix 5.11.

Specific optical rotation : Between +184° and +192°, determined in a 1.0 per cent w/v solution in *dioxan*, Appendix 5.12.

Light absorption : *Extinction* of a 1-cm layer of a 0.001 per cent w/v solution in *methyl alcohol* at the maximum at about 240 nm, between 0.365 and 0.395, ratio of *extinction* at the maximum at about 240 nm to that at 263 nm, between 1.85 and 2.05, Appendix 5.15 A.

Related foreign steroids : Complies with the test for *related foreign steroids, Method A*, Appendix 3.3.12.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 0.5 g by drying in an oven at 105°, for two hours, Appendix 5.8.

Assay : Carry out the **Assay** described under Betamethasone, using *prednisone acetate R.S.* for preparing the *standard solution*.

Storage : Store in well-closed, light-resistant containers.

Prednisone Tablets

Category : Adrenocortical steroid (anti-inflammatory).

Dose : Prednisone, 5 to 60 mg daily, in divided doses.

Usual strength : 5 mg; 10 mg.

Standards : Prednisone Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Prednisone, $C_{21}H_{26}O_5$.

Identification : (A) Shake a quantity of the powdered tablets equivalent to 15 mg of Prednisone with 5 ml of *chloroform* and evaporate the chloroform from the extract; the residue complies with **Identification** tests (A) and (B) described under Prednisone.

(B) The residue obtained in **Identification** test (A) complies with the list for *related foreign steroids, Method A*, Appendix 3.3.12.

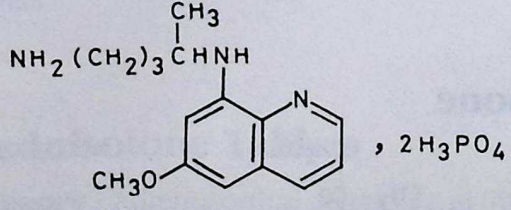
Uniformity of content : Comply with the tests described under Prednisolone Tablets.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Carry out the **Assay** described under Prednisolone Tablets, using *prednisone R.S.* for preparing the *standard solution*.

Storage : Store in well-closed, light-resistant containers.

Primaquine Phosphate



$C_{15}H_{21}N_3O, 2H_3PO_4$ Mol. Wt. 455.34

Category : Antimalarial.

Dose : The equivalent of 15 mg of Primaquine base, once a day for fourteen days.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Description : Orange-red, crystalline powder; odourless or almost odourless; taste, bitter.

Solubility : Soluble in *water*; insoluble in *chloroform*, and in *solvent ether*.

Standards : Primaquine Phosphate is the diorthophosphate of 8-(4-amino-1-methylbutylamino)-6-methoxyquinoline. It contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of $C_{15}H_{21}N_3O, 2H_3PO_4$, calculated with reference to the dried substance.

Identification : (A) The light absorption in the range 250 to 300 nm, of a 1-cm layer of a 0.0015 per cent w/v solution in *0.01N hydrochloric acid* exhibits two maxima, at 265 nm and 282 nm, *extinction* at 265 nm, about 0.5 and at 282 nm about 0.49, Appendix 5.15 A.

(B) Dissolve 10 mg in 5 ml of *water* and add 1 ml of a 5 per cent w/v solution of *ceric ammonium sulphate* in *dilute nitric acid*; a deep violet colour is immediately produced.

(C) Dissolve 50 mg in 5 ml of *water*, add 2 ml of *sodium hydroxide solution*, and extract with 2 quantities, each of 5 ml of *chloroform*. The aqueous layer after neutralisation with *dilute sulphuric acid* gives the reactions of *phosphates*, Appendix 3.1.,

(D) It melts at about 200°, Appendix 5.11.

pH : Between 2.5 and 3.5, determined in a 1.0 per cent w/v solution, Appendix 5.10.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 1.0 g and dissolve in 75 ml of *water*, add 10 ml of *hydrochloric acid* and carry out the *nitrite titration*, Appendix 3.3.4. Each ml of *0.1M sodium nitrite* is equivalent to 0.04553 g of $C_{15}H_{21}N_3O, 2H_3PO_4$.

Storage : Store in well-closed, light-resistant containers.

Primaquine Tablets

Primaquine Phosphate Tablets

Category : Antimalarial.

Dose : The equivalent of 15 mg of primaquine base daily, for fourteen days.

Usual strength : 2.5 mg.

Standards : Primaquine Tablets contain an amount of Primaquine Phosphate equivalent to not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of primaquine, $C_{15}H_{21}N_3O$. The tablets may be coated.

Identification : (A) Extract a quantity of the powdered tablets equivalent to 25 mg of primaquine with 10 ml of *water* and filter. To 2 ml of filtrate add 3 ml of *water* and 1 ml of a 5 per cent w/v solution of *ceric ammonium sulphate* in *dilute nitric acid*; a deep violet colour is immediately produced.

(B) Make the remainder of the filtrate obtained in **Identification** test (A) alkaline with *sodium hydroxide solution* and filter; the filtrate, after neutralisation with *dilute nitric acid*, gives the reactions of *phosphates*, Appendix 3.1.

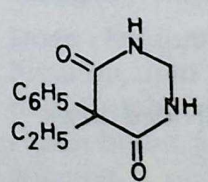
Uniformity of content : Powder one tablet, add 5 ml of *hydrochloric acid* and about 25 g of crushed ice, then add sufficient *water* to make the total volume to about 50 ml. Carry out the *nitrite titration*, Appendix 3.3.4, beginning at the words "cool to about 15°...." and using *0.01M sodium nitrite*. Carry out a blank determination and make any necessary correction. Each ml of *0.01M sodium nitrite* is equivalent to 2.594 mg of $C_{15}H_{21}N_3O$. Repeat the operation with a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 90 and 110 per cent of the average except that for one tablet the content may be between 85 and 115 per cent of the average.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 0.15 g of primaquine and dissolve in 50 ml of *water* by stirring. Filter and wash the residue with *water* until washings are no longer yellow. To the conbined filtrate and washings, add 5 ml of *hydrochloric acid* and carry out the *nitrite titration*, Appendix 3.3.4, beginning at the words "cool to about 15°....". Each ml of *0.1M sodium nitrite* is equivalent to 0.02594 g of $C_{15}H_{21}N_3O$.

Labelling : The label on the container states the strength in terms of the equivalent amount of primaquine.

Primidone



$C_{12}H_{14}N_2O_2$ Mol. Wt. 218.25

Category : Anticonvulsant.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Dose : 0.5 to 2 g daily, in divided doses.

Description : White crystalline powder, odourless; taste, slightly bitter.

Solubility : Very slightly soluble in *water*; slightly soluble in *alcohol*.

Standards : Primidone is 5-ethyl-5-phenylperhydropyrimidine-4,6-dione. It contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of $C_{12}H_{14}N_2O_2$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *primidone R.S.*, Appendix 5.15 B.

(B) Heat 0.5 g with 5 ml of *sulphuric acid (50 per cent v/v)*; odour of formaldehyde is produced.

(C) Dissolve 0.1 g in 5 ml of *chromotropic acid solution*, and heat in a water-bath for thirty minutes; a pinkish-blue colour develops.

(D) Fuse 0.2 g with 0.2 g of *anhydrous sodium carbonate*; ammonia is evolved.

Melting range : Between 279° and 284°, Appendix 5.11.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by heating in an oven at 130°, Appendix 5.8.

Assay : Weigh accurately about 0.2 g, add 100 ml of *alcohol* and boil gently to dissolve. Cool and add sufficient *alcohol* to produce 250.0 ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the minima at about 254 nm and at about 261 nm and the maximum at about 257 nm, Appendix 5.15 A. Correct the *extinction* at 257 nm by multiplying by 2 and then subtracting the *extinctions* obtained at 254 nm and 261 nm. Calculate the content of $C_{12}H_{14}N_2O_2$ from the corrected *extinction* obtained by repeating the assay on an accurately weighed quantity of *primidone R.S.* and from the declared content of $C_{12}H_{14}N_2O_2$ in the *primidone R.S.*

Storage : Store in well-closed containers.

Primidone Tablets

Category : Anticonvulsant.

Dose : Primidone, 0.5 to 2 g daily, in divided doses.

Usual strength : 0.25 g.

Standards : Primidone Tablets contain not less than 95.0 per cent, and not more than 105.0 per cent of the stated amount of Primidone, $C_{12}H_{14}N_2O_2$.

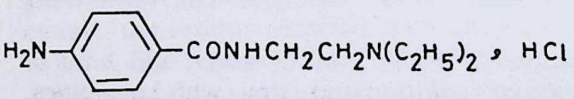
Identification : Extract the powdered tablets with hot *alcohol*, filter and evaporate the residue to dryness. The residue complies with the **Identification** tests (A) and (D) described under Primidone.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and finely powder 20 tablets. Weigh accurately a quantity of the powdered tablets equivalent to about 0.1 g of Primidone, add 100 ml of *alcohol* and boil gently. Cool and add sufficient *alcohol* to produce 250.0 ml. Complete the **Assay** described under Primidone, beginning at the words "Measure the *extinction*....".

Storage : Store in well-closed containers.

Procainamide Hydrochloride



$C_{13}H_{21}N_3O, HCl$ Mol. Wt. 271.79

Category : Myocardial depressant used in the treatment of arrhythmias.

Dose : 0.5 to 1.5 g.

Description : White to yellowish-white, crystalline powder; odourless. Hygroscopic.

Solubility : Very soluble in *water*; freely soluble in *alcohol*; slightly soluble in *chloroform* and very slightly soluble in *solvent ether*.

Standards : Procainamide Hydrochloride is the hydrochloride of 4-amino-*N*-(2-diethylaminoethyl) benzamide. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_{13}H_{21}N_3O, HCl$ calculated with reference to the dried substance.

Identification : (A) Dissolve 1 g in 10 ml of *water*, add 10 ml of *sodium hydroxide solution*, and extract with 10 ml of *chloroform*. To the extract add 10 ml of *toluene*, dry over *anhydrous sodium sulphate*, and filter. Mix the filtrate with 5 ml of dry *pyridine*, add 1 ml of *benzoyl chloride* drop by drop, heat on a water-bath for thirty minutes, and pour into a mixture of 50 ml of *water*, and 50 ml of *sodium hydroxide solution*. Extract with 10 ml of *solvent ether*, wash the extract with 20 ml of *water*, dilute with 30 ml of *solvent ether*, and allow to crystallise; the crystals after reprecipitation from *alcohol (45 per cent)*, melt at about 186°, Appendix 5.11.

(B) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.001 per cent w/v solution in *0.02 N*

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

sodium hydroxide exhibits a maximum at 275 nm; *extinction* at 275 nm, about 0.6, Appendix 5.15 A.

(C) A solution (1 in 10) gives the reactions of *chlorides*, Appendix 3.1.

Melting range : Between 165° and 169°, Appendix 5.11.

pH : Between 5.0 and 6.5, determined in a 10 per cent w/v solution, Appendix 5.10.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 70 volumes of *chloroform*, 30 volumes of *methyl alcohol* and 0.7 volumes of *strong ammonia solution* as the mobile phase. Apply separately to the plate 10 µl of each of two solutions in *methyl alcohol* containing (1) 2.0 per cent w/v of the substance being examined and (2) 0.010 per cent w/v of the substance being examined. Add to each point of application 10 µl of a 20 per cent w/v solution of *strong ammonia solution* in *methyl alcohol*. After removal of the plate, allow it to dry in air and spray with *ethanolic dimethylaminobenzaldehyde solution*. Any spot in the chromatogram obtained with solution (1), other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (2).

Heavy metals : Not more than 20 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.5 g, dissolve in 75 ml of *water*, add 10 ml of *hydrochloric acid*, and carry out the *nitrite titration*, Appendix 3.3.4. Each ml of *0.1M sodium nitrite* is equivalent to 0.02718 g of $C_{13}H_{21}N_3O$, HCl.

Storage : Store in well-closed containers.

Procainamide Injection

Procainamide Hydrochloride Injection

Category : Cardiac depressant (anti-arrhythmic)

Dose : Procainamide Hydrochloride. By slow intravenous injection of a 2.5 per cent w/v solution, upto 1 g, in accordance with the effects produced.

Usual strength : 100 mg per ml.

Standards : Procainamide Injection is a sterile solution of Procainamide Hydrochloride in Water for Injection, containing 0.9 per cent v/v of Benzyl Alcohol and 0.1 per cent w/v of Sodium Metabisulphite. It contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of $C_{13}H_{21}N_3O$, HCl.

Description : Clear, colourless or almost colourless solution.

Identification : (A) Dilute with *water* to produce a solution containing 0.0005 per cent w/v of Procainamide Hydrochloride; *extinction* of a 1-cm layer at 280 nm, about 0.30, Appendix 5.15 A.

(B) It gives the reactions of *chlorides*, Appendix 3.1.

pH : Between 4.5 and 6.0, Appendix 5.10.

Related substances : Complies with the test described under Procainamide Hydrochloride, using the following two solutions: For solution (1) dilute a volume of the injection equivalent to 0.1 g of Procainamide Hydrochloride to 5 ml with *methyl alcohol*; for solution (2) dilute 1 volume of solution (1) to 100 volumes with *methyl alcohol*.

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using a dose of 0.5 ml per kg of the rabbit's weight containing 0.1 g of Procainamide Hydrochloride per ml.

Other requirements : Comply with the requirements stated under Injections.

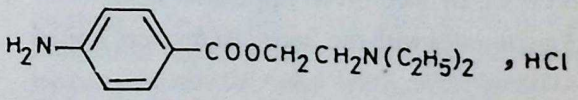
Assay : Carry out the **Assay** described under Procainamide Hydrochloride using an accurately measured volume equivalent to about 0.5 g of Procainamide Hydrochloride.

Storage : Store in single-dose or multiple-dose containers.

Labelling : The label on the container states 'Not to be used if the solution is discoloured'.

Procaine Hydrochloride

Ethocaine Hydrochloride



$C_{13}H_{20}N_2O_2$, HCl Mol. Wt. 272.77

Category : Local anaesthetic.

Dose : Epidural, 25 ml of a 1.5 per cent solution. Infiltration, upto 200 ml of a 0.25 to 0.5 per cent solution. Peripheral nerve block, upto 25 ml of a 2 per cent solution. Spinal, 1 to 3 ml of a 3.3 to 5 per cent solution.

Description : Colourless crystals or white crystalline powder; odourless; taste, slightly bitter followed by a sensation of numbness.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Solubility : Very soluble in *water*; soluble in *alcohol*; slightly soluble in *chloroform*; practically insoluble in *solvent ether*.

Standards : Procaine Hydrochloride is the hydrochloride of 2-diethylaminoethyl-*p*-aminobenzoate. It contains not less than 99.0 per cent of $C_{13}H_{20}N_2O_2$,HCl, calculated with reference to the dried substance.

Identification : (A) Dissolve 0.1 g in 5 ml of *water*, add two drops of *dilute sulphuric acid* and then five drops of *0.1N potassium permanganate*; the colour of the latter is immediately discharged (distinction from cocaine hydrochloride).

(B) A solution gives a precipitate with *potassium mercuri-iodide solution* (distinction from benzocaine and orthocaine).

(C) Dissolve 10 mg in 1 ml of *water*; add one drop of *hydrochloric acid*, one drop of a 10 per cent w/v solution of *sodium nitrite* and 1 ml of a 10.0 per cent w/v solution of *2-naphthol* in *sodium hydroxide solution* and shake; a scarlet-red precipitate is formed.

(D) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

(E) A 10 per cent w/v solution does not give any precipitate with 0.5 per cent w/v solution of *sodium bicarbonate*; but with *sodium hydroxide solution*, it yields a colourless oily precipitate which becomes crystalline on standing. The precipitate after washing with *water* and drying at 100° and allowing to solidify, melts at about 60°, Appendix 5.11.

Melting range : Between 153° and 158°, Appendix 5.11.

pH : Between 5.0 and 6.5, determined in a 2.0 per cent w/v solution, Appendix 5.10.

Clarity and colour of solution : A 5.0 per cent w/v solution is clear and colourless.

Heavy metals : Not more than 40 parts per million, determined on 0.5 g by Method A, Appendix 3.2.4.

Iron : 0.25 g complies with the *limit test for iron*, Appendix 3.2.5.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not mote than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 1 g and dissolve in 20 ml of *water*; add 5 ml of *hydrochloric acid*, and carry out the *nitrite titration*, Appendix 3.3.4. Perform a blank determination and make any necessary correction. Each ml of *0.1M sodium nitrite* is equivalent to 0.02728 g of $C_{13}H_{20}N_2O_2$,HCl.

Storage : Store in well-closed, light-resistant containers.

Procaine and Adrenaline Injection

Procaine Hydrochloride and Adrenaline Injection; Procaine Hydrochloride and Epinephrine Injection

Category : Local anaesthetic.

Standards : Procaine and Adrenaline Injection contains not less than 1.9 per cent w/v and not more than 2.1 per cent w/v of Procaine Hydrochloride, $C_{13}H_{20}N_2O_2$, HCl and the equivalent of not less than 0.00175 per cent w/v and not more than 0.00225 per cent w/v of Adrenaline, $C_9H_{13}NO_3$.

Procaine Hydrochloride	2 g
Sodium Chloride	0.5 g
Chlorocresol	0.1 g
Adrenaline Solution*	2 ml
Sodium Metabisulphite	0.1 g
Water for Injection sufficient to produce	100 ml

Dissolve the Chlorocresol in about 90 ml of Water for Injection with the aid of gentle heat. Cool, dissolve the Procaine Hydrochloride, the Sodium Metabisulphite and the Sodium Chloride in the solution, and add the Adrenaline Solution and sufficient Water for Injection to produce 100 ml. Distribute the solution into suitable containers, seal and sterilise by heating for sufficient length of time to ensure that the solution in each container is maintained at 98° to 100° for thirty minutes.

* Adrenaline Solution may be prepared in the following manner:

Adrenaline Bitartrate	1.8 g
Chlorbutol	4 g
Chlorocresol	1 g
Sodium Metabisulphite	1 g
Sodium Chloride	8 g
Purified Water sufficient to produce	1000 ml

Dissolve the Sodium Metabisulphite in 100 ml of Purified Water and add the Adrenaline Bitartrate. Dissolve the Chlorbutol and the Chlorocresol in 750 ml of Purified Water with the aid of gentle heat. Cool and dissolve the Sodium Chloride in the solution. Mix the two solutions and add sufficient purified water to produce 1000 ml.

Description : Clear and colourless solution.

Identification : (A) To 5 ml add 5 ml of *water* and 10 ml of *picric acid solution*; shake gently and set aside for one

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

hour; the crystalline precipitate, after washing with *water* and drying at 195° melts at about 134°, Appendix 5.11.

(B) To 5 ml add 1 ml of *hydrochloric acid*, cool to 0°, add 5 ml of *sodium nitrite solution* and pour the mixture into 2 ml of *2-naphthol solution* containing 1 g of *sodium acetate*; an orange-red colour is produced.

(C) Complies with **Identification** test (B) described under Lignocaine and Adrenaline Injection.

pH : Between 3.0 and 5.5, Appendix 5.10.

Other requirements : Comply with the requirements stated under Injections.

Assay : *For Procaine Hydrochloride* – To 10 ml add 0.5 g of *sodium carbonate* and extract with three quantities, each of 20 ml, of a mixture of 1 volume of *isopropyl alcohol* and 3 volumes of *chloroform* until complete extraction of procaine is effected. Shake the combined extracts with 5 ml of *water*, wash the water with the mixture of *isopropyl alcohol* and *chloroform* and add the washing to the combined extracts. Shake the combined extracts and washings with 10 ml of *0.1N hydrochloric acid*, separate the acid layer, wash the combined extracts and washings with 5 ml of *water*, add the aqueous extract to the separated acid layer and titrate with *0.1N sodium hydroxide*, using *methyl red-methylene blue solution* as indicator. Each ml of *0.1N hydrochloric acid* is equivalent to 0.02728 g of $C_{13}H_{20}N_2O_2$,HCl.

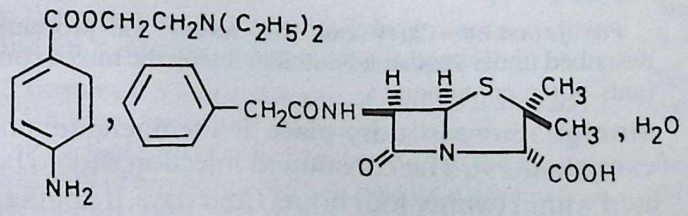
For adrenaline – Carry out the **Assay** *for adrenalin* described under Lignocaine and Adrenaline Injection, using 10 ml.

Storage : Store in single-dose or multiple-dose, light-resistant containers.

Labelling : The label on the container states the strength as "Procaine Hydrochloride, 2 per cent; Adrenaline, 1 in 50,000".

Procaine Penicillin

Procaine Benzylpenicillin; Procaine Penicillin G



$C_{13}H_{20}N_2O_2, C_{16}H_{18}N_2O_4S, H_2O$ Mol. Wt. 588.72

Category : Antibacterial.

Dose : By intramuscular injection, 0.3 to 0.9 g daily. 0.3 g is approximately equivalent to 0.2 g of benzylpenicillin.

Description : White, crystalline powder.

Solubility : Slightly soluble in *water*.

Standards : Procaine Benzylpenicillin is the monohydrate of 2-(4-aminobenzoyloxy) ethyldiethyl ammonium-(6*R*)-6-(2-phenylacetamido) penicillanate. It contains not less than 96.0 per cent of total penicillins, calculated as $C_{13}H_{20}N_2O_2, C_{16}H_{18}N_2O_4S, H_2O$ and not less than 37.5 per cent and not more than 40.5 per cent of procaine, $C_{13}H_{20}N_2O_2$.

Identification : (A) A solution at pH 6.0 to 7.0, at 37°, is inactivated under suitable conditions by *penicillinase solution*.

(B) Dissolve 0.1 g in 2 ml of *dilute hydrochloric acid* with the aid of heat if necessary, cool in ice, and add 4 ml of a 1.0 per cent w/v solution of *sodium nitrite*, and pour the mixture in 2 ml of *β-naphthol solution* containing 1 g of *sodium acetate*; a bright orange-red precipitate is produced.

pH : Between 5.0 and 7.5, determined in a 30 per cent w/v suspension in *water*, Appendix 5.10.

Water : Not more than 4.2 per cent w/w, Appendix 3.3.25.

Assay : *For total penicillins*–Weigh accurately about 75 mg, dissolve in 50.0 ml of *water*, add 10.0 ml of *sodium silicotungstate solution*, shake, allow to stand for three minutes, and filter. Carry out the remainder of the assay as quickly as possible. Transfer 10.0 ml of the filtrate to a stoppered flask, add 5 ml of *N sodium hydroxide*, and allow to stand for thirty minutes; add 5.5 ml of *N hydrochloric acid* and 30.0 ml of *0.02N iodine*, close the flask with a wet stopper, allow to stand for fifteen minutes, protected from light, and titrate the excess of iodine with *0.02N sodium thiosulphate*, using *starch solution*, added towards the end of the titration, as indicator. To a further 10.0 ml of the filtrate add 30.0 ml of *0.02N iodine* and titrate immediately with *0.02N sodium thiosulphate*, using *starch solution*, added towards the end of the titration, as indicator. The difference between the titrations represents the volume of *0.02N iodine* equivalent to the total penicillins present. Calculate the content of total penicillins from the difference obtained by carrying out the assay using *benzylpenicillin sodium R.S.* instead of the substance being examined. Each mg of *benzylpenicillin sodium R.S.* is equivalent to 1.652 mg of total penicillins, calculated as $C_{13}H_{20}N_2O_2$, $C_{16}H_{18}N_2O_4S,H_2O$.

For procaine–Weigh accurately about 0.1 g, add 20 ml of *water* and 5 ml of *sodium carbonate solution* and extract with successive quantities, each of 25 ml, of *chloroform* until complete extraction of the procaine is effected, washing each *chloroform* extract with the same 5 ml of *water*. Shake the mixed chloroform extracts in succession with 20.0 ml of *0.01N sulphuric acid* and 5 ml of *water* and titrate the excess of acid in the combined acid

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

and aqueous layers with *0.01N sodium hydroxide*, using *methyl red solution* as indicator. Each ml of *0.01N sulphuric acid* is equivalent to 0.002363 g of $C_{13}H_{20}N_2O_2$.

Procaine Penicillin intended for parenteral administration complies with the following additional requirements:

Pyrogens : Complies with the *test for pyrogens*, Appendix 2.36, using a quantity not less than 1.5 mg per kg of the rabbit's weight dissolved in not more than 5 ml of *water for injection*.

Sterility : Complies with the *test for sterility*, Appendix 4.6.

Undue toxicity : Complies with the test described under Bacitracin, the dose being 0.5 ml of a suspension containing the equivalent of 0.75 mg of total penicillins in 0.5 ml of *saline solution*.

Storage : Store in well-closed, containers at a temperature not exceeding 30°. If it is intended for parenteral administration the container should be sterile and sealed so as to exclude micro-organisms.

Labelling : The label on the container states (1) the date after which the contents are not intended to be used; (2) the storage conditions; (3) whether or not the contents are intended for parenteral administration.

Fortified Procaine Penicillin Injection

Procaine Penicillin with Benzylpenicillin Injection

Category : Antibacterial.

Dose : The dose is determined by the physician in accordance with the needs of the patient.

Usual strength : Procaine Penicillin 0.3 g (300,000 Units) and Benzylpenicillin 60 mg (100,000 Units).

Standards : Fortified Penicillin Injection is a sterile suspension of Procaine Penicillin in Water for Injection containing Benzylpenicillin in solution. It is prepared by adding the requisite amount of Water for Injection to the contents of a sealed container which contains a mixture of five parts of Procaine Penicillin and one part of Benzylpenicillin, together with suitable dispersing agents. The sealed container may contain a suitable buffering agent.

Content of total penicillins—Determine the weight of the contents of each of ten containers as described in the test for **Uniformity of weight** under Injections. From the result of the **Assay** for the content of total penicillins, calculate the proportionate amount of total penicillins in each container. This amount is not less than 60.0 per cent and not more than 74.0 per cent of the total content of Procaine Penicillin and Benzylpenicillin stated on the label except that in one container the amount may be not less than 54.0 per cent and not more than 80.0 per cent of the content of Procaine Penicillin and Benzylpenicillin stated on the label.

Content of procaine, $C_{13}H_{20}N_2O_2$—From the result of the **Assay** for the content of procaine, calculate the proportionate amount of procaine, $C_{13}H_{20}N_2O_2$ in each of the ten containers, the weight of contents of which has been determined in the test for content of total penicillins. This amount is not less than 36.0 per cent and not more than 44.0 per cent of the content of Procaine Penicillin stated on the label except that in one container the amount may be not less than 32.0 per cent and not more than 48.0 per cent of the content of Procaine Penicillin stated on the label.

Other requirements : Complies with the requirements stated under Injections.

The contents of the sealed container comply with the following requirements:

Description : White or almost white powder; practically odourless.

Identification; Pyrogens; Sterility; Undue toxicity : Comply with the requirements stated under Procaine Penicillin.

Consistence : To a quantity equivalent to 0.3 g (300,000 Units) of Procaine Penicillin and 60 mg (100,000 Units) of Benzylpenicillin add 1.0 ml of *water* and shake thoroughly. The resulting suspension passes readily through a 22 G hypodermic needle.

Water : Not more than 3.5 per cent w/w, determined on 0.6 g, Appendix 3.3.25.

Assay : *For total penicillins*—Carry out the **Assay** for total penicillins described under Procaine Penicillin, using 70 mg, accurately weighed, of the mixed contents of ten containers. Each mg of *benzylpenicillin sodium R.S.* is equivalent to 1.000 mg of total penicillins, calculated as $C_{16}H_{17}N_2NaO_4S$.

For procaine—Carry out the **Assay** for procaine described under Procaine Penicillin, using the mixed contents of ten containers.

Storage : Store in a dry place at a temperature not exceeding 25°. The constituted injection should be used within twenty-four hours (four days, if a buffering agent is present) when stored at a temperature not exceeding 20° or within seven days (fourteen days, if a buffering agent is present) when stored in a cold place.

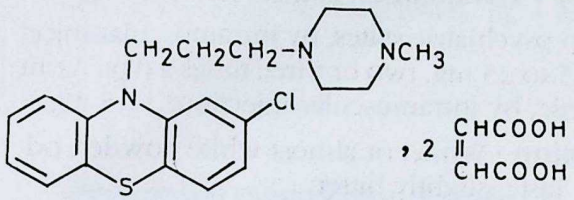
Labelling : The label on the sealed container states (1) the quantity of Procaine Penicillin and Benzyl-

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

penicillin in g and in Units contained in it; (2) the names of any added dispersing and buffering agent; (3) "For intramuscular injection only"; (4) the date after which the contents are not intended to be used; (5) the storage conditions.

Prochlorperazine Maleate



$C_{20}H_{24}ClN_3S,2C_4H_4O_4$ Mol. Wt. 606.09

Category : Tranquilliser; anti-emetic.

Dose : As tranquilliser, 15 to 100 mg daily, in divided doses. As an anti-emetic, 10 to 30 mg.

Description : White or pale-yellow, crystalline powder; almost odourless; taste, slightly bitter.

Solubility : Almost insoluble in *water*, and in *alcohol*; insoluble in *solvent ether*.

Standards : Prochlorperazine Maleate is the dihydrogen maleate of 2-chloro-10-[3-(4-methylpiperazin-1-yl)propyl] phenothiazine. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_{20}H_{24}ClN_3S, 2C_4H_4O_4$, calculated with reference to the dried substance.

Identification : (A) The light absorption in the range 240 to 350 nm, of a 1-cm layer of 0.001 per cent w/v solution in *ethyl alcohol* containing 0.01 per cent v/v of *strong ammonia solution* exhibits a maximum at 258 nm and a less well defined maximum at 313 nm; *extinction* at 258 nm, about 0.6, Appendix 5.15 A.

(B) Dissolve 5 mg in 2 ml of *sulphuric acid* and allow to stand for 5 minutes; a red colour is produced.

(C) Dissolve 0.3 g in a mixture of 3 ml of *water* and 2 ml of *sodium hydroxide solution*, shake with three portions each of 3 ml of *solvent ether*. Add to the aqueous solution 2 ml of *bromine solution*. Warm on a water-bath for ten minutes, then heat to boiling, cool and add two drops of a solution of 10 mg of *resorcinol* in 3 ml of *sulphuric acid*; a bluish-black colour develops on heating for fifteen minutes in a water-bath.

(D) Carry out in subdued light the method for *thin-layer chromatography*, Appendix 5.4.3, using *kieselguhr G* as the coating substance. Impregnate the dry plate by placing it in a tank containing a shallow layer of a mixture of 10 volumes of *2-phenoxyethanol*, 5 volumes of *polyethylene glycol 400* and 85 volumes of *acetone*; allowing the impregnating solvent to ascend to the top, removing the plate from the tank, and using it immediately. Use as the mobile phase a mixture of 2 volumes of *diethylamine* and 100 volumes of *light petroleum (boiling range 40° to 60°)* saturated with *2-phenoxyethanol*. Apply separately to the plate 2 µl of each of the following solutions. Solution (1) is a 0.2 per cent w/v solution of the substance being examined in a mixture of equal volumes of *chloroform* and *methyl alcohol* containing 0.5 per cent v/v of *strong ammonia solution*; solution (2) is a 0.2 per cent w/v solution of *prochlorperazine maleate R.S.* in the same solvent. After removal of the plate, allow it to dry in air, examine under an ultra-violet lamp having a maximum output at about 366 nm, and observe the fluorescence produced after about two minutes. Spray the plate with a 10 per cent v/v solution of *sulphuric acid* in *alcohol* and observe the colour produced. The principal spot in the chromatogram obtained with solution (1) corresponds in position, fluorescence, and colour to that in the chromatogram obtained with solution (2). Under ultra-violet light a secondary spot, due to maleic acid, is observed in both the chromatograms.

Melting range : Between 198° and 203°, Appendix 5.11.

Foreign substances : Carry out in subdued light and in an atmosphere of *nitrogen* the method for *thin-layer chromatography*, Appendix 5.4.3, using a suitable silica gel as the coating substance and a mixture of 80 volumes of *cyclohexane*, 10 volumes of *acetone* and 10 volumes of *diethylamine* as the mobile phase. Apply separately to the plate 10 µl of each of two freshly prepared solutions in a mixture of 95 volumes of *methyl alcohol* and 5 volumes of *diethylamine* containing (1) 2.0 per cent w/v of the substance being tested, and (2) 0.01 per cent w/v solution of the substance being tested. After removal of the plate allow it to dry in air and examine under an untra-violet lamp having a maximum output at about 254 nm. Any spot obtained in the chromatogram with solution (1), other than the principal spot is not more intense than the spot in the chromatogram obtained with solution (2).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.6 g, and dissolve in 20 ml of *glacial acetic acid*, add a few drops of *crystal-violet solution* and titrate with *0.1N perchloric acid*. Perform a blank determination and make by necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.03030 g of $C_{20}H_{24}ClN_3S, 2C_4H_4O_4$.

Storage : Store in well-closed, light-resistant containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Prochlorperazine Injection

Category : Tranquilliser; anti-emetic.

Dose : In psychiatric states, by intramuscular injection, 12.5 to 25 mg two or three times a day. As an anti-emetic, by intramuscular injection, 12.5 mg.

Usual strength : 12.5 mg per ml.

Description : Colourless or almost colourless liquid.

Standards : Prochlorperazine Injection is a sterile solution of Prochlorperazine Mesylate in Water for Injection, free from dissolved air, containing suitable buffering and stabilising agents. It contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of $C_{20}H_{24}ClN_3S, 2CH_3SO_3H$.

Identification : (A) To a volume equivalent to 5 mg of Prochlorperazine Mesylate, carefully add 2 ml of *sulphuric acid* and allow to stand for five minutes, a red colour is produced.

(B) To a volume equivalent to 0.2 g of Prochlorperazine Mesylate, add 1.5 ml of *sodium hydroxide solution* and extract with 10 ml of *solvent ether*. Wash the ether layer with two quantities, each of 5 ml of *water* and evaporate to dryness. Dissolve the residue in 10 ml of *methyl alcohol*, and add a solution of 0.3 g of *picric acid* in a mixture of 5 ml of *methyl alcohol* and 5 ml of *water*. The precipitate, after washing with 15 ml of *methyl alcohol*, melts at about 255°, with decomposition, Appendix 5.11.

pH : Between 5.5 and 6.5, Appendix 5.10.

Other requirements : Complies with the requirements stated under Injections.

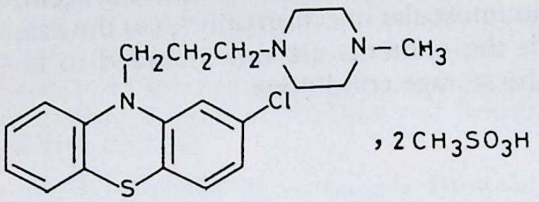
Assay : Protect the solution from light throughout the assay.

To an accurately measured volume equivalent to 12.5 mg Prochlorperazine Mesylate, add sufficient *ethyl alcohol* containing 0.01 per cent of *strong ammonia solution* to produce 100.0 ml. Dilute 5.0 ml of the solution to 100.0 ml with the ammoniacal alcohol and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 258 nm, Appendix 5.15 A. Calculate the content of $C_{20}H_{24}ClN_3S, 2CH_3SO_3H$, taking 635 as the value of E(1 per cent, 1-cm) at the maximum at about 258 nm.

Storage : Store in light-resistant containers.

Labelling : The label on the container states "Do not use the Injection if it is discoloured".

Prochlorperazine Mesylate



$C_{20}H_{24}ClN_3S, 2CH_3SO_3H$ Mol. Wt. 566.15

Category : Tranquilliser; anti-emetic.

Dose : In psychiatric states, by intramuscular injection, 12.5 to 25 mg, two or three times a day. As an anti-emetic, by intramuscular injection, 12.5 mg.

Description : White, or almost white powder; odourless; taste, slightly bitter.

Solubility : Very soluble in *water*; sparingly soluble in *alcohol*; slightly soluble in *chloroform*; insoluble in *solvent ether*.

Standards : Prochlorperazine Mesylate is dimethanesulphonate of 2-chloro-10-[3-(4-methylpiperazin-1-yl) propyl] phenothiazine. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_{20}H_{24}ClN_3S, 2CH_3SO_3H$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are at the same wavelengths as and have similar relative intensities to, those in the spectrum of *prochlorperazine mesylate R.S.*, Appendix 5.15 B.

(B) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.0007 per cent w/v solution in *ethyl alcohol* containing 0.01 per cent v/v of *strong ammonia solution* exhibits a maximum at 258 nm and a less well defined maximum at about 313 nm; *extinction* at 258 nm, about 0.44, Appendix 5.15 A.

(C) Complies with **Identification** test (B) described under Prochlorperazine Maleate.

(D) Complies with **Identification** test (D) described under Phentolamine Mesylate.

pH : Between 2.0 and 3.0, determined in a 2.0 per cent w/v solution, Appendix 5.10.

Foreign substances : Complies with the test described under Prochlorperazine Maleate.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying "in vacuo at 100°," Appendix 5.8.

Assay : Weigh accurately about 0.8 g, dissolve in 10 ml of *water*, add 5 ml of *N sodium hydroxide* and extract with

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

successive quantities of 50, 25, 25 and 20 ml of *solvent ether*. Wash the combined ether extracts with 5 ml of *water*, shake the washings with 5 ml of *solvent ether*, add the ether to the combined ether extracts, and evaporate the solvent. Add 2 ml of *ethyl alcohol* to the residue, evaporate to dryness, add 20 ml of *glacial acetic acid*, a few drops of *crystal-violet solution* and titrate with *0.1N perchloric acid*. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02831 g of $C_{20}H_{24}ClN_3S, 2CH_3SO_3H$.

Storage : Store in well-closed, light-resistant containers.

Prochlorperazine Tablets

Category : Tranquilliser; anti-emetic.

Dose : In psychiatric states, 15 to 100 mg daily, in divided doses; as an anti-emetic, 10 to 30 mg.

Standards : Prochlorperazine Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Prochlorperazine Maleate, $C_{20}H_{24}ClN_3S, 2C_4H_4O_4$.

Identification : (A) Shake a quantity of the powdered tablets equivalent to 0.2 g of Prochlorperazine Maleate, with 2 ml of *water* and 1 ml of *sodium hydroxide solution*, mix and extract with three quantities, each of 10 ml, of *solvent ether*. Dry the combined extracts with *anhydrous sodium sulphate*, filter, evaporate to dryness and dissolve the residue in 10 ml of *methyl alcohol*, and add a solution of 0.15 g of *picric acid* in 10 ml of *methyl alcohol*. Melting point of the precipitate, after washing with few ml of *methyl alcohol*, about 255°, with decomposition, Appendix 5.11.

(B) To a quantity of the powdered tablets equivalent to about 5 mg of Prochlorperazine Maleate add 5 ml of *sulphuric acid* and allow to stand for five minutes; a red colour is produced.

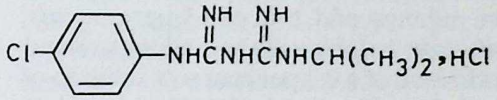
Other requirements : Comply with the requirements stated under Tablets.

Assay : Protect the solution from light throughout the assay; weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 25 mg of Prochlorperazine Maleate and extract with three quantities, each of 10 ml, of *ethyl alcohol* containing 0.01 per cent v/v of *strong ammonia solution*. Filter the extract and to the combined filtrates add sufficient quantity of the ammoniacal alcohol to produce 100.0 ml. Dilute 10.0 ml to 50.0 ml with *ethyl alcohol*, dilute 10.0 ml of this solution to 50.0 ml with *ethyl alcohol*, and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 258 nm, Appendix 5.15A. Calculate the content of $C_{20}H_{24}ClN_3S, 2C_4H_4O_4$ taking 620 as the value of E(1 per cent, 1-cm) at the maximum at about 258 nm.

Storage : Store in light-resistant containers.

Proguanil Hydrochloride

Chloroguanide Hydrochloride



$C_{11}H_{16}ClN_5, HCl$ Mol. Wt. 290.19

Category : Antimalarial.

Dose : As a suppressant of malaria, 0.1 to 0.3 g, daily.

Description : White, crystalline powder; odourless; taste, bitter.

Solubility : Slightly soluble in *water*; more soluble in hot *water*; soluble in *alcohol*; practically insoluble in *chloroform* and in *solvent ether*.

Standards : Proguanil Hydrochloride is the hydrochloride of 1-(4-chlorophenyl)-5-isopropylbiguanide. It contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of $C_{11}H_{16}ClN_5, HCl$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *proguanil hydrochloride R.S.*, Appendix 5.15B.

(B) To 10 ml of a saturated solution, add five drops of *potassium ferrocyanide solution*; a white precipitate is produced which dissolves on addition of a few drops of *dilute nitric acid*.

(C) To 10 ml of saturated solution, add one drop of *copper sulphate solution*, shake well, add 5 ml of *toluene*, and again shake; the *toluene* layer is coloured purplish-red.

(D) Dissolve 5 mg in 5 ml of a warm 1.0 per cent w/v solution of *cetrimide* and add 1 ml of *sodium hydroxide solution* and 1 ml of *bromine solution*; a deep red colour is produced.

(E) A solution (1 in 200) gives the reactions of *chlorides*, Appendix 3.1.

Melting range : Between 244° and 246°, Appendix 5.11.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Acidity or Alkalinity : To 350 ml of *water* at 60° to 65°, add 0.2 ml of *methyl red and methylene blue solution* and neutralise with *0.1N sodium hydroxide* or *0.1N hydrochloric acid*, add 4 g of the substance being examined and dissolve at 60° to 65°; the solution is not acid, and requires for neutralisation not more than 0.2 ml of *0.1N hydrochloric acid.*

Heavy metals : Not more than 20 parts per million determined on 1.0 g by Method C, Appendix 3.2.4.

Chloroaniline : Dissolve 0.10 g in 1 ml of *dilute hydrochloric acid* and add sufficient *water* to produce 20 ml; cool to 5°, add 1 ml of *0.05M sodium nitrite*, and allow to stand at 5° for five minutes; add 2 ml of a 5 per cent w/v solution of *ammonium sulphamate* and allow to stand for ten minutes; add 2 ml of a 0.1 per cent w/v solution of *N-(1-naphthyl)-ethylenediamine hydrochloride*, dilute to 50 ml with *water*, and allow to stand for thirty minutes. The magenta colour produced is not deeper than that given by 25 µg of *4-chloroaniline* under the same conditions.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g, by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.3 g, dissolve in 25 ml of *glacial acetic acid*, and 10 ml of *mercuric acetate solution* and titrate with *0.1N perchloric acid*, determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.01451 g of $C_{11}H_{16}ClN_5$, HCl.

Storage : Store in well-closed, light-resistant containers.

Proguanil Tablets

Proguanil Hydrochloride Tablets; Chloroguanide Hydrochloride Tablets

Category : Antimalarial.

Dose : Proguanil Hydrochloride. As a suppressant of malaria, 0.1 to 0.3 g daily.

Usual strength : 0.1 g.

Standards : Proguanil Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Proguanil Hydrochloride, $C_{11}H_{16}ClN_5$, HCl.

Identification : (A) Boil a quantity of the powdered tablets equivalent to 0.5 g of Proguanil Hydrochloride with 5 ml of *dilute hydrochloric acid*, cool, and filter. To the filtrate add a slight excess of *sodium hydroxide solution*, and evaporate the ethereal extract, the residue, after drying at 105° melts at about 131°, Appendix 5.11.

(B) Dissolve the residue obtained in **Identification** test (A) in the minimum quantity of *dilute hydrochloric acid*; the solution diluted with *water* to about 40 ml and neutralised if necessary, with cautious addition of *dilute ammonia solution*, complies with **Identification** tests (C) and (D) described under Proguanil Hydrochloride.

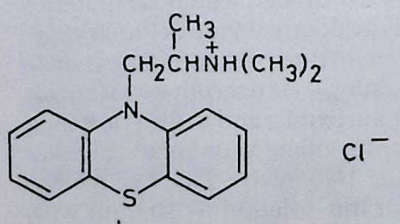
Chloroaniline : To a quantity of the powdered tablets equivalent to 0.1 g of Proguanil Hydrochloride add 5 ml of *alcohol* and shake for ten minutes. Add 2.5 ml of *2N hydrochloric acid* and 15 ml of *water*, mix and filter through a wetted filter paper, washing the filter with 5 ml of *water*. The filtrate complies with the test described under Proguanil Hydrochloride, beginning at the words "cool to 5°.....".

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. To a quantity of the powder equivalent to 0.1 g of Proguanil Hydrochloride add 5 ml of *water* and warm on a water-bath with stirring until a smooth paste is obtained. Add 50 ml of *water*, continue warming for ten minutes, cool, add sufficient *water* to produce 100.0 ml and filter. Dilute 10.0 ml of the filtrate to 100.0 ml with *water* and to 10.0 ml of the resulting solution add 70 ml of *water*, 5 ml of a 20 per cent w/v solution of *cetrimide* and 1 ml of *isopropyl alcohol*. Adjust the temperature of the solution to 20° and add 2 ml of *alkaline sodium hypobromite solution* and sufficient *water* to produce 100.0 ml. Allow to stand at 20° for twenty-five minutes and measure the *extinction* of the resulting solution at the maximum at about 480 nm, Appendix 5.15 A. Calculate the content $C_{11}H_{16}ClN_5$, HCl from the *extinction* obtained by repeating the operation using 10 ml of a 0.01 per cent w/v solution of *proguanil hydrochloride R.S.* beginning at the words "add 70 ml of *water*...." and from the declared content of $C_{11}H_{16}ClN_5$,HCl in *proguanil hydrochloride R.S.*

Storage : Store in well-closed, light-resistant containers.

Promethazine Hydrochloride



$C_{17}H_{20}N_2S$, HCl Mol. Wt. 320.88

Category : Antihistaminic; anti-emetic.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Dose : 20 to 50 mg daily, in single or divided doses.

Description : White or faintly cream-coloured, crystalline powder; odourless or almost odourless; taste, very bitter.

Solubility : Very soluble in *water*; freely soluble in *alcohol* and in *chloroform*; practically insoluble in *solvent ether*.

Standards : Promethazine Hydrochloride is *N,N*-dimethyl[1-methyl-2-(phenothiazin-10yl)ethyl] ammonium chloride. It contains not less than 98.5 per cent and not more than the equivalent of 101.0 per cent of $C_{17}H_{20}N_2S$, HCl calculated with reference to the dried substance.

Identification : (A) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.0005 per cent w/v solution in *0.01N hydrochloric acid* exhibits a maximum at 249 nm and a less well-defined maximum at about 300 nm; *extinction* at 249 nm, about 0.45, Appendix 5.15 A.

(B) Carry out in subdued light the method for *thin-layer chromatography*, Appendix 5.4.3, using *kieselguhr G* as the coating substance. Impregnate the dry plate by placing it in a tank containing a shallow layer of a mixture of 10 volumes of *2-phenoxyethanol*, 5 volumes of *macrogol 400*, and 85 volumes of *acetone*, allowing the impregnating solvent to ascend to the top, removing the plate from the tank, and using it immediately. Use as the mobile phase a mixture of 2 volumes of *diethylamine* and 100 volumes of *light petroleum (boiling range 40° to 60°)* saturated with *2-phenoxyethanol*. Apply separately to the plate 2 µl of each of two solutions in *chloroform* containing (1) 0.2 per cent w/v of the substance being examined and (2) 0.2 per cent w/v of *promethazine hydrochloride R.S.* After removal of the plate, allow it to dry in air, examine under an ultra-violet lamp having a maximum output at about 366 nm, and observe the fluorescence produced after about two minutes. Spray the plate with a 10 per cent v/v solution of *sulphuric acid* in *alcohol* and observe the colour produced. The principal spot in the chromatogram obtained with solution (1) corresponds in position, fluorescence and colour to that in the chromatogram obtained with solution (2).

(C) Dissolve about 5 mg in 5 ml of *sulphuric acid*; a cherry-red colour is produced which darkens slowly on standing. On warming a portion of this solution, the colour changes through brown to magenta; the remaining portion, on addition of 0.2 ml of *0.1N potassium dichromate*, changes to brownish-red.

(D) To 0.5 g dissolved in 10 ml of *water* add 4 ml of *nitric acid*; a red colour and a red precipitate which redissolves are produced; on warming, the colour of the solution changes to orange-yellow.

(E) A solution (1 in 20) gives the reactions of *chlorides*, Appendix 3.1.

Melting range : Between 221° and 225°, Appendix 5.11.

pH : Between 3.5 and 5.0, determined in a freshly-prepared 10 per cent w/v solution, Appendix 5.10.

Related impurities : Carry out the test for *thin-layer chromatography* under an atmosphere of nitrogen, Appendix 5.4.3, using *silica gel GR 254* as the coating substance and a mixture of 85 volumes of *hexane*, 10 volumes of *acetone* and 5 volumes of *diethylamine* as the mobile phase. Apply separately to the plate 10 µl of each of three freshly-prepared solutions in a mixture of 95 volumes of *methyl alcohol* and 5 volumes of *diethylamine* containing (1) 2.0 per cent of the substance being examined; (2) 0.02 per cent w/v of *isopromethazine hydrochloride R.S.* and (3) 0.01 per cent w/v of *promethazine hydrochloride R.S.* After removal of the plate allow it to dry in air and examine under an ultra-violet lamp having a maximum output at about 254 nm. The spot in the chromatogram obtained with solution (2) is more intense than any corresponding spot in the chromatogram obtained with solution (1). Any spot in the chromatogram obtained with solution (1), apart from the principal spot is not more intense than the spot in the chromatogram obtained with solution (3).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.6g, dissolve in 200 ml of *acetone* and add 10 ml of *mercuric acetate solution*, titrate with *0.1N perchloric acid* using 3 ml of a saturated solution of *methyl orange* in *acetone* as indicator. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.03209 g of $C_{17}H_{20}N_2S$, HCl.

Storage : Store in well-closed, light-resistant containers.

Promethazine Tablets

Promethazine Hydrochloride Tablets

Category : Antihistaminic; anti-emetic.

Dose : Promethazine Hydrochloride, 20 to 50 mg daily, in single or divided doses.

Usual strengths : 10 mg, 25 mg and 50 mg.

Standards : Promethazine Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Promethazine Hydrochloride, $C_{17}H_{20}N_2S$, HCl. The tablets are coated.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Identification : (A) Comply with **Identification** test (B) described under Promethazine Hydrochloride applying to the plate 2 µl of each of the following solutions. For solution (1) shake a quantity of the powdered tablets with sufficient *chloroform* to produce a solution containing the equivalent of 2 mg of Promethazine Hydrochloride per ml, centrifuge, and use the supernatant liquid; solution (2) is a 0.2 per cent w/v solution of *promethazine hydrochloride R.S.* in *chloroform.*

(B) The powdered tablets comply with **Identification** tests (C), (D) and (E) described under Promethazine Hydrochloride.

Related impurities : Comply with the test described under Promethazine Hydrochloride, but using the following solutions, freshly prepared: (1) Extract a quantity of the powdered tablets equivalent to 0.1 g of Promethazine Hydrochloride with 10 ml of a mixture of 95 volumes of *methyl alcohol* and 5 volumes of *diethylamine* and filter; (2) a 0.01 per cent w/v solution of *isopromethazine hydrochloride R.S.* in a mixture of 95 volumes of *methyl alcohol* and 5 volumes of *diethylamine*; (3) a solution prepared by diluting 1 volume of solution (1) to 200 volumes with a mixture of 95 volumes of *methyl alcohol* and 5 volumes of *diethylamine.* The spot in the chromatogram obtained with solution (2) is more intense than any corresponding spot in the chromatogram obtained with solution (1). Any spot in the chromatogram obtained with solution (1) other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (3).

Uniformity of content (for 10 mg tablets only) : Crush one tablet, add 1 ml of *dilute hydrochloric acid* and 30 ml of *water* and shake for fifteen minutes. Add sufficient *water* to produce 50.0 ml and centrifuge. Complete the **Assay** beginning at the words "To 5.0 ml of the clear supernatant liquid.....". Calculate the content of $C_{17}H_{20}N_2S$, HCl.

Repeat the operation using a further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 85 per cent and 115 per cent of the average except that for one tablet the content may be between 80 per cent and 120 per cent of the average.

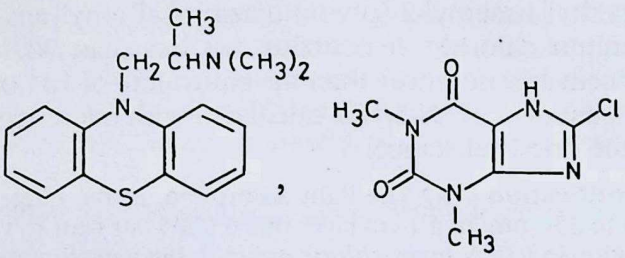
Other requirements : Comply with the requirements stated under Tablets.

Assay : Protect the solutions from light throughout the assay.

Weigh and powder 20 tablets. Weigh accurately a quantity of the powdered tablets equivalent to 50 mg of Promethazine Hydrochloride, add 5 ml of *dilute hydrochloric acid* and 200 ml of *water.* Shake for fifteen minutes, add sufficient *water* to produce 500.0 ml and centrifuge 50 ml of the mixture. To 5.0 ml of the clear, supernatant liquid add 10 ml of *0.1N hydrochloric acid* and sufficient *water* to produce 100.0 ml. Measure the *extinction* of the resulting solution at the maximum at about 249 nm, Appendix 5.15 A. Calculate the content of $C_{17}H_{20}N_2S$, HCl, taking 910 as the value of E(1 per cent, 1-cm) at the maximum at about 249 nm.

Storage : Store in well-closed, light-resistant containers.

Promethazine Theoclate



$C_{17}H_{20}N_2S, C_7H_7ClN_4O_2$ Mol. Wt. 499.04

Category : Antihistamine.

Dose : 25 to 50 mg daily, in single or divided doses.

Description : White or almost white powder; odourless; taste, slightly bitter.

Solubility : Very slightly soluble in *water*; sparingly soluble in *alcohol*; freely soluble in *chloroform*; insoluble in *solvent ether.*

Standards : Promethazine Theoclate is the promethazine salt of 8-chlorotheophylline. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_{17}H_{20}N_2S, C_7H_7ClN_4O_2$, calculated with reference to the dried substance.

Identification : (A) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.0007 per cent w/v solution in *ethyl alochol* containing 0.01 per cent v/v of *strong ammonia solution* exhibits a maximum at 255 nm; *extinction* at 255 nm, about 0.56, Appendix 5.15 A.

(B) Dissolve 5 mg in 2 ml of *sulphuric acid* and allow to stand for 5 minutes; a red colour is produced.

(C) Shake 0.4 g with 10 ml of *water*, add 4 ml of *dilute ammonia solution* and shake with two quantities, each of 30 ml, of *solvent ether.* Add to the aqueous solution 4 ml of *hydrochloric acid*; a white, precipitate is produced, which after washing with *water*, complies with the following tests:

(a) Dissolve 10 mg in 1 ml of *hydrochloric acid*, add 0.1 g of *potassium chlorate*, and evaporate to dryness; a reddish residue is obtained which becomes purple on exposure to *dilute ammonia solution.*

(b) Fuse 50 mg with 0.5 g of *anhydrous sodium carbonate*, boil the residue with 5 ml of *water*, acidify to *litmus paper* with *nitric acid* and filter. The filtrate gives the reactions of *chlorides*, Appendix 3.1.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Chloride : Shake 2.0 g with 20 ml of *water* for two minutes and filter; 10 ml of the filtrate complies with the *limit test for chlorides*, Appendix 3.2.2.

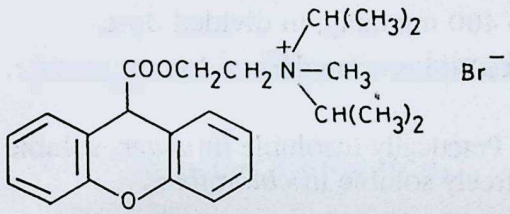
Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 1.0g and dissolve in 200 ml of *acetone*. Add 3 ml of a saturated solution of *methyl orange* in *acetone* and titrate with *0.1N perchloric acid*. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.0499 g of $C_{17}H_{20}N_2S,C_7H_7ClN_4O_2$.

Storage : Store in well-closed, light-resistant containers.

Propantheline Bromide



$C_{23}H_{30}BrNO_3$ Mol. Wt. 448.40

Category : Anticholinergic.

Dose : Up to 45 mg daily, in divided doses.

Description : White or yellowish-white crystals or powder; odourless; taste, very bitter. Slightly hygroscopic.

Solubility : Very soluble in *water*, in *alcohol* and in *chloroform*; practically insoluble in *solvent ether* and in *benzene*.

Standards : Propantheline Bromide is *N,N*-di-isopropyl-*N*-methyl-2-(xanthen-9-ylcarbonyloxy)ethylammonium bromide. It contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of $C_{23}H_{30}BrNO_3$, calculated with reference to the dried substance.

Identification : (A) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.006 per cent w/v solution in *methyl alcohol* exhibits two maxima, at 246 nm and 282 nm; *extinction* at 246 nm, about 0.7, and at 282 nm, about 0.37, Appendix 5.15 A.

(B) Dissolve 0.2 g in 15 ml of *water*, add 2 ml of *sodium hydroxide solution*, boil for two minutes, cool slightly, add 5ml of *dilute hydrochloric acid*, cool, and filter. The residue, after washing with *water*, recrystallisation from *alcohol (50 per cent)*, and drying at 105° for one hour, melts at about 215°, Appendix 5.11.

(C) To 10 mg of the crystals obtained in **Identification** test (B), add 5 ml of *sulphuric acid*; a bright yellow solution is produced which fluoresces strongly in ultra-violet light.

(D) A solution (1 in 20) gives the reactions of *bromides*, Appendix 3.1.

Melting range : between 156° and 162°, determined on a sample dried at 105° for four hours, Appendix 5.11.

Xanthanoic acid and xanthone : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3 using *silica gel G* as the coating substance and a mixture of 140 volumes of *ethylene chloride*, 60 volumes of *methyl alcohol*, 2.5 volumes of *water* and 2.5 volumes of *formic acid* as the mobile phase but allowing the solvent front to ascend 10 cm above the line of application. Apply separately to the plate 25 µl of each of solutions in *chloroform* containing (1) 0.5 per cent w/v substance being examined and (2) 0.0025 per cent w/v of *xanthanoic acid R.S.* and (3) 0.0025 per cent w/v of the *xanthone R.S.* After removal of the plate, allow it to dry in air, and spray with a mixture of 1 volume of *sulphuric acid* and 2 volumes of *water*. Heat at 85° for fifteen minutes, cool and examine under an ultra-violet lamp having a maximum out-put at about 254 nm. Any spots in the chromatogram other than the principal spot obtained with solution (1) are less intense than the corresponding spots, in the chromatogram obtained with solution (2) and (3).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.6 g and dissolve in a mixture of 20 ml of *glacial acetic acid* and 15 ml of *mercuric acetate solution*, warming slightly if necessary to effect solution. Cool and titrate with *0.1N perchloric acid*, determining the end point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.04484 g of $C_{23}H_{30}BrNO_3$.

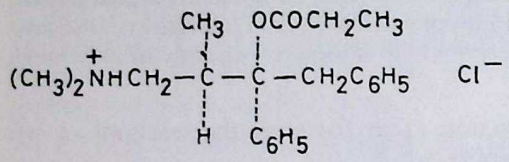
Storage : Store in well-closed containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Dextropropoxyphene Hydrochloride

Propoxyphene Hydrochloride



$C_{22}H_{29}NO_2, HCl$ Mol. Wt. 375.94

Category : Analgesic.

Dose : Upto 260 mg daily in divided doses.

Description : White or slightly yellow powder; odourless; taste, bitter.

Solubility : Freely soluble in *water*; soluble in *alcohol*, in *chloroform*, and in *acetone*; practically insoluble in *benzene*, and in *solvent ether*.

Standards : Dextropropoxyphene Hydrochloride is the (2*R*,3*S*)-2-methyl-3,4-diphenyl-3-propionyloxybutyl-*N*,*N*'-dimethylammonium chloride. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_{22}H_{29}NO_2, HCl$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *dextropropoxyphene hydrochloride R.S.*, Appendix 5.15 B.

(B) Dissolve 25 mg in 5 ml of *water*, evaporate one drop of the solution in a porcelain dish and streak the spot with *sulphuric acid* containing one drop of *formaldehyde solution* per ml; a purple colour is produced.

(C) A solution (1 in 20) gives the reaction of *chlorides*, Appendix 3.1.

Melting range : Between 163.5° and 168.5°, Appendix 5.11.

Specific optical rotation : Between +52° and +57°, determined on a freshly prepared 10 per cent w/v solution and calculated with reference to the dried substance, Appendix 5.12.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

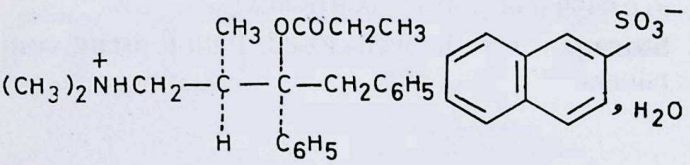
Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105° for 3 hours, Appendix 5.8.

Assay : Weigh accurately about 0.6 g, dissolve in 40 ml of *glacial acetic acid* and add 10 ml of *mercuric acetate solution*. Add *crystal-violet solution* and titrate with *0.1N perchloric acid* to a green end-point. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.03759 g of $C_{22}H_{29}NO_2, HCl$.

Storage : Store in well-closed containers.

Dextropropoxyphene Napsylate

Propoxyphene Napsylate



$C_{22}H_{29}NO_2, C_{10}H_8O_3S, H_2O$ Mol. Wt. 565.72

Category : Analgesic.

Dose : Upto 400 mg daily, in divided doses.

description : White powder; odourless; taste, bitter.

Solubility : Practically insoluble in *water*; soluble in *alcohol*; freely soluble in *chloroform*.

Standards : Dextropropoxyphene Napsylate is monohydrate of (2*R*,3*S*)-2-methyl-3,4-diphenyl-3-propionyloxybutyl-*N*,*N*-dimethylammonium naphthalene-2-sulphonate. It contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of $C_{22}H_{29}NO_2, C_{10}H_8O_3S$, calculated with reference to the anhydrous substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at same wavelengths as, and have similar relative intensities to, those in the spectrum of *dextropropoxyphene napsylate R.S.*, Appendix 5.15 B.

(B) Dissolve 25 mg in 5 ml of *chloroform*, evaporate one drop of the solution in a porcelain dish, and streak the spot with *sulphuric acid* containing one drop of *formaldehyde solution* per ml; a purple colour is produced.

(C) Burn 20 mg by the *oxygen flask method*, Appendix 3.3.6. using 5 ml of *dilute sodium hydroxide solution* as the absorbing liquid. When the process is complete, dilute the liquid to 25 ml with *water*. To the 5 ml solution thus obtained, add 1 ml of *strong hydrogen peroxide solution*, 1 ml *N hydrochloric acid* and mix well and add 0.05 ml of *barium chloride solution* ; a turbidity is produced.

(D) It melts at about 160°, Appendix 5.11.

Specific optical rotation : Between +35° and +43°,

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

determined in a 1.0 per cent w/v solution in *chloroform*, Appendix 5.12.

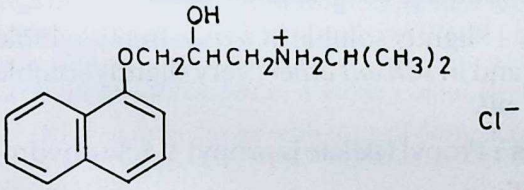
Water : 3.0 to 5.0 per cent w/w, Appendix 3.3.25.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Assay : Weigh accurately about 0.75 g and disperse in 50 ml of *water*, by swirling, and add 5 ml of *sodium hydroxide solution*. Extract with five quantities, each of 25 ml of *chloroform*. Wash each extract with the same 20 ml of *water*. Dry the combined extracts with *anhydrous sodium sulphate*, evaporate to about 3 ml on a water-bath in a current of air. Remove from the water-bath and allow to evaporate to dryness at room temperature. Dissolve the residue in about 40 ml of *glacial acetic acid*. Add *crystal violet solution* and titrate with *0.1N perchloric acid*. Carry out a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.05477 g of $C_{22}H_{29}NO_2$, $C_{10}H_8O_3S$.

Storage : Store in well-closed containers.

Propranolol Hydrochloride



$C_{16}H_{21}NO_2$, HCl Mol. Wt. 295.81

Category : Adrenergic, β-receptor antagonist (antihypertensive, anti-anginal; anti-arrhythmic).

Dose : 20 mg to 2 g daily, in divided doses; the initial daily dose should not exceed 40 mg; by slow intravenous injection, 3 to 10 mg.

Description : White or almost white powder; odourless; taste, bitter.

Solubility : Soluble in *water* and in *alcohol*; slightly soluble in *chloroform*.

Standards : Propranolol Hydrochloride is *N*-[2-hydroxy-3-(1-naphthyloxy)propyl] isopropylammonium chloride. It contains not less than 99.0 per cent of $C_{16}H_{21}NO_2$, HCl, calculated with reference to the dried substance.

Identification : (A) Dissolve 0.2 g in 6 ml of *water*, heating gently, if necessary, make alkaline with *sodium hydroxide solution* and extract with two quantities each of 5 ml of *solvent ether*. Wash the combined extracts with *water* until the washings are free from alkali, dry with *anhydrous sodium sulphate*, filter and evaporate to dryness. The residue, after drying under vacuum at 50° for one hour, melts at about 94°, Appendix 5.11.

(B) The light absorption in the range 230 to 350 nm, of a 1-cm layer of a 0.002 per cent w/v solution in *methyl alcohol* exhibits maxima at 290 nm, 306 nm and 319 nm. *Extinction* at 290 nm, about 0.42, at 360 nm, about 0.25, and at 319 nm, about 0.15, Appendix 5.15 A.

(C) Dissolve 0.1 g in 5 ml of *water* and add a few ml of *silver nitrate solution*; a white curdy precipitate is produced which is insoluble in *nitric acid* but is soluble after it is washed well with *water*, in *dilute ammonia solution*.

pH : Between 5.0 and 6.0, determined in 1.0 per cent w/v solution, Appendix 5.10.

Related substances : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 90 volumes of toluene and 10 volumes of *methyl alcohol* as the mobile phase. Apply separately to the plate 10 µl of each of two solutions in *methyl alcohol* containing (1) 10 per cent w/v of the substance being examined; (2) 0.02 per cent w/v of the substance being examined. After removal of the plate, allow it to dry in air, spray with a mixture of 0.5 ml of *anisaldehyde*, 10 ml of *glacial acetic acid*, 85 ml of *methyl alcohol* and 5 ml of *sulphuric acid* and heat at 105° for 15 minutes. Any spot in the chromatogram obtained with solution (1), other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (2).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.7 g and dissolve in 80 ml of *glacial acetic acid*, add 10 ml of *mercuric acetate solution* and a drop of *1-naphtholbenzein solution*; titrate with *0.1N perchloric acid* to a dark green endpoint. Carry out a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02958 g of $C_{16}H_{21}NO_2$,HCl.

Storage : Store in well-closed containers.

Propranolol Tablets

Category : Anti-adrenergic, cardiac depressant (anti-arrhythmic).

Dose : Propranolol Hydrochloride, 20 mg to 2 g daily, in divided doses; the initial dose should not exceed 40 mg.

Usual strengths : 10 mg; 40 mg.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Standards : Propranolol Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of Propranolol Hydrochloride, $C_{16}H_{21}NO_2$, HCl.

Identification : (A) The light absorption of the solution obtained in the **Assay** exhibits maxima at 290 nm, 306 nm and 319 nm, Appendix 5.15 A.

(B) The powdered tablets comply with **Identification** test (C) described under Propranolol Hydrochloride.

(C) Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and *methyl alcohol* containing 1 per cent v/v of *strong ammonia solution* as the mobile phase. Apply separately to the plate 10 µl of each of the following solutions. For solution (1) suspend a quantity of the powdered tablets equivalent to 10 mg of Propranolol Hydrochloride in 10 ml of *water*, make alkaline with *sodium hydroxide solution*, and extract with 5 ml of *chloroform*. Solution (2) is a 0.2 per cent w/v solution of *propranolol hydrochloride R.S.* in *chloroform*. After removal of the plate, allow it to dry in air for a few minutes and spray with a solution prepared by mixing equal volumes of a 0.3 per cent w/v solution of *platinic chloride* and a 6 per cent w/v solution of *potassium iodide* immediately before use. The spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

Uniformity of content (for tablets containing 10 mg): Transfer one tablet to a 100-ml volumetric flask, add 5 ml of *dilute hydrochloric acid* and allow to stand, swirling occasionally, until it is disintegrated. Add about 70 ml of *methyl alcohol* and shake well for about a minute. Dilute to volume with *methyl alcohol*, mix, and centrifuge a portion of the solution. Dilute a suitable volume of the clear solution with *methyl alcohol* to produce a solution containing 40 µg of Propranolol Hydrochloride per ml. Measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 290 nm, Appendix 5.15 A, using *methyl alcohol* as the blank. Calculate the content of $C_{16}H_{21}NO_2$, HCl, taking 210 as the value of E(1 per cent, 1-cm) at the maximum at about 290 nm.

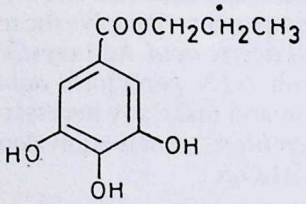
Repeat the operation with a further nine tablets and calculate the average content of ten tablets. The content of each tablet is between 90 and 110 per cent of the average except that for one tablet the content may be between 85 and 115 per cent of the average.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 20 mg of Propranolol Hydrochloride and shake with 60 ml of *methyl alcohol* for ten minutes, add sufficient *methyl alcohol* to produce 100.0 ml, and filter. Dilute 10.0 ml of the filtrate to 100.0 ml with *methyl alcohol* and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 290 nm, Appendix 5.15 A. Calculate the content of $C_{16}H_{21}NO_2$,HCl, taking 210 as the value of E(1 per cent, 1-cm) at the maximum at about 290 nm.

Storage : Store in well-closed, light-resistant containers.

Propyl Gallate



$C_{10}H_{12}O_5$ Mol. Wt. 212.20

Category : Pharmaceutical aid (anti-oxidant).

Description : White to creamy-white crystalline powder; odourless; taste, slightly bitter.

Solubility : Slightly soluble in *water*; freely soluble in *alcohol* and in *solvent ether*; very slightly soluble in *arachis oil*.

Standards : Propyl Gallate is propyl 3,4,5-trihydroxybenzoate.

Identification : (A) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.001 per cent w/v solution in *methyl alcohol* exhibits a maximum only at 275 nm; *extinction* at 275 nm, about 0.49, Appendix 5.15 A.

(B) Dissolve 10 mg in 5 ml of hot *water*, cool and add 5 ml of *dilute ammonia solution*; a red colour is produced which becomes brown on standing and is restored on shaking.

(C) Dissolve 5 mg in 50 ml of *water* and add 0.05 ml of *ferric chloride test-solution*; a bluish-black colour is produced.

Melting range : Between 146° and 148°, Appendix 5.11.

Chloride : Shake 2.0 g with 50 ml of *water* for five minutes and filter; 25 ml of the filtrate complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphate : Shake 1.0 g with 50 ml of *water* for five minutes and filter; 25 ml of the filtrate complies with the *limit test for sulphates*, Appendix 3.2.8.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

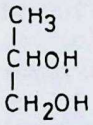
Loss on drying : Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Storage : Store in well-closed, light-resistant containers, free from contact with metals.

Propylene Glycol



$C_3H_8O_2$ Mol. Wt. 75.09

Category : Pharmaceutical aid (humectant; solvent).

Description : Clear, colourless, viscous liquid; practically odourless; taste, slightly sweet; hygroscopic.

Solubility : Miscible with *water*, with *acetone* and with *chloroform*; soluble in *solvent ether*.

Standards : Propylene Glycol is propane-1,2-diol.

Identification : (A) To 0.5 ml of a 0.01 per cent w/v solution, cooled in ice, add 5 ml of a cooled mixture of 10 ml of *water* and 90 ml of *sulphuric acid*. Heat for ten minutes on a water-bath at 70°, cool and add 0.2 ml of a 3 per cent w/v solution of *ninhydrin* in a 2.5 per cent w/v solution of *sodium metabisulphite*. A violet colour slowly appears.

(B) Heat three drops with 0.1 g of *boric acid*. A pleasant odour develops.

(C) Add 1 ml to 0.5 g of *potassium bisulphate* and heat gently; a fruity odour develops and when the solution is heated to dryness no sharp, acrid odour of acrolein is perceptible.

Boiling range : Between 184° and 189°, Appendix 5.3.

Specific gravity : Between 1.035 and 1.037, Appendix 5.19.

Acidity or Alkalinity : Mix 10 ml with 40 ml of *water*, add a few drops of *bromothymol blue solution* and titrate with *0.1N sodium hydroxide* or with *0.1N hydrochloric acid*; not more than 0.2 ml is required.

Chloride : 2.0 g complies with the *limit test for chlorides*, Appendix 3.2.2.

Sulphate : 1.0 g complies with the *limit test for sulphates*, Appendix 3.2.8.

Arsenic : Not more than 5 parts per million, Appendix 3.2.1.

Heavy metals : Not more than 10 parts per million, determined on 2 ml by Method A, Appendix 3.2.4.

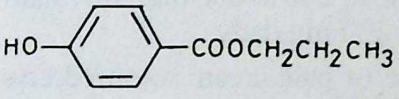
Sulphated ash : Not more than 0.01 per cent, determined in the following manner: Heat 50 g until it ignites and allow it to burn without further application of heat; cool, moisten the residue with *sulphuric acid* and ignite to constant weight.

Water : Not more than 0.2 per cent w/v, Appendix 3.3.25.

Storage : Store in tightly-closed containers.

Propylparaben

Propyl Parahydroxybenzoate; Propylhydroxybenzoate



$C_{10}H_{12}O_3$ Mol. Wt. 180.20

Category : Pharmaceutical aid (antifungal preservative).

Description : White crystalline powder; odourless; tasteless.

Solubility : Very slightly soluble in *water*; freely soluble in *alcohol*, in *acetone* and in *solvent ether*.

Standards : Propylparaben is propyl-4-hydroxybenzoate. It contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of $C_{10}H_{12}O_3$, calculated with reference to the dried substance.

Identification : (A) The light absorption, in the range 220 to 350 nm, of a 1-cm layer of a 0.0005 per cent w/v solution exhibits a maximum at 258 nm, Appendix 5.15 A.

(B) Complies with **Identification** tests (A) and (B) described under Methylparaben.

Melting range : Between 95° and 98°, Appendix 5.11.

Acidity; Chloride; Sulphate; Sulphated ash : Complies with the requirements described under Methylparaben.

Loss on drying : Not more than 0.5 per cent determined on 1.0 g, by drying over *silica gel* for five hours, Appendix 5.8.

Assay : Carry out the **Assay** described under Methylparaben. Each ml of *0.1N bromine* is equivalent to 0.003003 g of $C_{10}H_{12}O_3$.

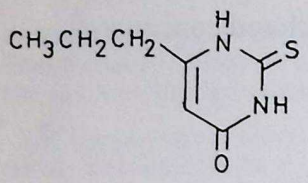
Storage : Store in well-closed containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Propylthiouracil

Propacil



$C_7H_{10}N_2OS$ Mol. Wt. 170.23

Category : Thyroid inhibitor.

Dose : Controlling dose, 200 to 600 mg daily. Maintenance dose, 50 to 200 mg daily.

Description : White or pale cream-coloured crystals or crystalline powder; odourless; taste bitter.

Solubility : Very slightly soluble in *water*; sparingly soluble in *alcohol*; slightly soluble in *chloroform* and in *solvent ether*. Soluble in solutions of ammonia and of alkali hydroxides.

Standards : Propylthiouracil is the 2,3-dihydro-6-propyl-2-thioxo-4-pyrimidinone. It contains not less than 98.0 per cent of $C_7H_{10}N_2OS$, calculated with reference to the dried substance.

Identification : (A) 25 mg dissolves completely in 1 ml of *strong ammonia solution* (distinction from thiouracil).

(B) To about 25 mg in a test-tube, add *bromine solution*, drop by drop, until solution is complete. Warm until the colour is discharged, cool, and add 10 ml of *barium hydroxide solution*; a permanent white precipitate is produced (distinction from thiouracil which yields a white precipitate that turns purple within one minute).

(C) To a boiling saturated solution, add an equal volume of a fresh aqueous solution containing 0.4 per cent w/v of *sodium nitroprusside*, 0.4 per cent w/v of *hydroxylamine hydrochloride* and 0.8 per cent w/v of *sodium bicarbonate*; a greenish blue colour is produced.

Melting range : Between 218° and 221°, Appendix 5.11.

Arsenic : Not more than 5 parts per million, Appendix 3.2.1.

Heavy metals : Not more than 20 parts per million, determined on 1.0 g by Method B, Appendix 3.2.4.

Thiourea : Boil 0.5 g with 50 ml of *water* under a reflux condenser until dissolved and dilute 5 ml of the hot solution to 50 ml with *water*. Place 10 ml of this solution in a test-tube (A) and add 1 ml of a 0.01 per cent w/v solution of *thiourea*. Cool the remainder of the hot solution, filter and place 10 ml of the filtrate in second test-tube (B) To each tube add 0.5 g of *sodium acetate* and 5 ml of *0.1N silver nitrate* and heat in a water-bath for five minutes. The colour of the liquid in tube (B) is not darker than that of the liquid in tube (A).

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.4 g and dissolve in a mixture of 50 ml of *0.1N sodium hydroxide* and 200 ml of *water*. Warming to complete the solution. Cool, add 10 g of *sodium acetate*, acidify the solution to *litmus paper* with *acetic acid*, add 1 ml of a freshly prepared 0.5 per cent w/v solution of *diphenylcarbazone* in *alcohol*, and titrate with *0.05M mercuric acetate* until a rose-violet colour persists for two to three minutes. Each ml of *0.05M mercuric acetate* is equivalent to 0.01702 g of $C_7H_{10}N_2OS$.

Storage : Store in well-closed, light-resistant containers.

Propylthiouracil Tablets

Propacil Tablets

Category : Thyroid inhibitor.

Dose : Propylthiouracil. Controlling dose, 200 to 600 mg daily; maintenance dose, 50 to 200 mg daily.

Usual strength : 50 mg.

Standards : Propylthiouracil Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the labelled amount of Propylthiouracil, $C_7H_{10}N_2OS$.

Identification : Extract a quantity of the powdered tablets in a continuous extraction apparatus with *solvent ether*, and evaporate the solution to dryness; the residue, after drying at 105°, melts at about 219 °, Appendix 5.11, and complies with **Identification** test (A) to (C), described under Propylthiouracil.

Other requirements : Comply with the requirements stated under Tablets.

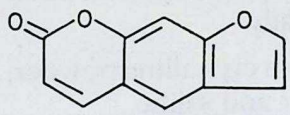
Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 0.4 g of Propylthiouracil and carry out the **Assay** described under Propylthiouracil.

Storage : Store in well-closed, light-resistant containers.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Psoralen



$C_{11}H_6O_3$ Mol. Wt. 186.14

Category : Topical pigmenting agent.

Description : Colourless needles; odourless tasteless.

Solubility : Very soluble in *chloroform*; soluble in *alcohol*; sparingly soluble in *solvent ether*; practically insoluble in *light petroleum (boiling range 60° to 80°)*.

Standards : Psoralen is furo (3,2-g) coumarin obtained from the fruit of *Psoralea carylifolia* Linn. (Fam. Leguminosae) and from the leaves of *Ficus carica* (Fam. Urticaceae) or prepared by synthesis. It contains not less than 95.0 per cent of $C_{11}H_6O_3$, calculated with reference to the dried substance.

Identification : (A) Dissolve 1 mg in 5 ml of *alcohol* and add 15 ml of a mixture containing 3 volumes of *propylene glycol*, 5 volumes of *acetic acid*, and 43 volumes of *water*; a blue fluorescence is visible under ultra-violet light.

(B) Dissolve 1 mg in 2 ml of *alcohol* and add 2 drops of *0.1N sodium hydroxide*; a yellow fluorescence is visible under ultra-violet light.

Melting range : Between 162° and 165°, Appendix 5.11.

Related compounds : Carry out the method for *thin-layer chromatography*, Appendix 5.4.3, using *silica gel G* as the coating substance and a mixture of 9 volumes of *benzene* and 1 volume of *ethyl acetate* as the mobile phase. Apply separately to the plate 5 µl of each of two solutions in *chloroform* containing (1) 20 mg of the substance being examined per ml and (2) 1 ml of solution (1) diluted to 100 ml with *chloroform*. Allow to dry and examine under an ultra-violet lamp having maximum output at about 366 nm. Any spot in the chromatogram with solution (1), other than the principal spot, is not more intense than the spot in the chromatogram obtained with solution (2).

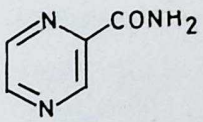
Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 1.0 per cent, determined by drying 1.0 g in an oven at 100°, Appendix 5.8.

Assay : Weigh accurately about 0.1 g, dissolve in sufficient *methyl alcohol* to produce 100.0 ml; dilute 2.0 ml to 100.0 ml with *methyl alcohol* and measure the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 247 nm, Appendix 5.15 A. Calculate the content of $C_{11}H_6O_3$, from the *extinction* obtained by repeating the **Assay** on 20 mg, accurately weighed, of *psoralen R.S.* and from the declared content of $C_{11}H_6O_3$ in the *psoralen R.S.*

Storage : Store in well-closed, light-resistant containers.

Pyrazinamide



$C_5H_5N_3O$ Mol. Wt. 123.11

Category : Tuberculostatic.

Dose : Upto 35 mg per kg of body weight daily, in divided doses.

Description : White or almost white crystalline powder; odourless or almost odourless; taste, slightly bitter.

Solubility : Sparingly soluble in *water*; slightly soluble in *alcohol*; soluble in *solvent ether*, and in *chloroform*.

Standards : Pyrazinamide is pyrazine-2-carboxamide. It contains not less than 99.0 per cent of $C_5H_5N_3O$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *pyrazinamide R.S.*, Appendix 5.15 B.

(B) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.001 per cent w/v solution exhibits two maxima, at 268 nm and 310 nm; *extinction* at 268 nm, about 0.66, and at 310 nm, about 0.06, Appendix 5.15 A.

(C) Boil 20 mg with 5 ml of *sodium hydroxide solution*; ammonia, recognisable by its odour, is evolved.

Melting range : Between 188° and 191°, Appendix 5.11.

Heavy metals : Not more than 10 parts per million, determined on 2.0 g by Method B, Appendix 3.2.4.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7

Water : Not more than 0.5 per cent, Appendix 3.3.25.

Assay : Weigh accurately about 0.3 g and transfer to the flask of an ammonia distillation apparatus. Add 200 ml of *water* and 75 ml of *sodium hydroxide solution*. Gently boil for 20 minutes, collecting the distillate in 50 ml of

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

0.1N sulphuric acid. Boil vigorously to complete the distillation of the ammonia and titrate the excess of acid with *0.1N sodium hydroxide*, using *methyl red solution* as indicator. Repeat the operation without pyrazinamide; the difference between the two titrations represents the acid required to neutralise the ammonia formed from the pyrazinamide. Each ml of *0.1N sulphuric acid* is equivalent to 0.01231 g of $C_5H_5N_3O$.

Storage : Store in well-closed containers.

Pyrazinamide Tablets

Category : Tuberculostatic.

Dose : Pyrazinamide, upto 35 mg per kg of body weight daily, in divided doses.

Usual strengths : 250 mg; 500 mg; 750 mg.

Standards : Pyrazinamide Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Pyrazinamide, $C_5H_5N_3O$.

Identification : (A) Shake a quantity of the powdered tablets equivalent to 50 mg of Pyrazinamide with 50 ml of *water* and filter. The filtrate, after necessary dilution complies with **Identification** test (B) described under Pyrazinamide.

(B) Boil a quantity of the powdered tablets equivalent to 20 mg of Pyrazinamide with 5 ml of *sodium hydroxide solution*; ammonia, recognisable by its odour, is evolved.

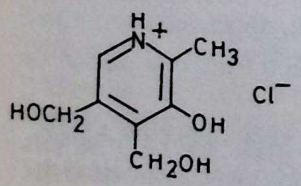
Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to 0.3 g of Pyrazinamide. Carry out the **Assay** described under Pyrazinamide.

Storage : Store in well-closed containers.

Pyridoxine Hydrochloride

Vitamin B_6



$C_8H_{12}ClNO_3$ Mol. Wt. 205.64

Category : B-group vitamin.

Dose : Prophylactic, 2 mg daily; therapeutic, 10 to 150 mg one to three times daily.

Description : White or whitish crystalline powder; odourless; taste, slightly bitter and saline.

Solubility : Freely soluble in *water*; sparingly soluble in *alcohol*; practically insoluble in *chloroform* and in *solvent ether*.

Standards : Pyridoxine Hydrochloride is 3-hydroxy-4,5-bis-(hydroxymethyl)-2-methylpyridinium chloride. It contains not less than 98.5 per cent of $C_8H_{12}ClNO_3$, calculated with reference to the dried substance.

Identification : (A) Place 1 ml of a 0.01 per cent w/v solution into each of two test-tubes. To each tube add 2 ml of a 20 per cent w/v solution of *sodium acetate*. To the first tube add 1 ml of *water* and to the second tube add 1 ml of a 4 per cent w/v solution of *boric acid*, mix. Cool both the tubes to about 20° and rapidly add to each tube 1 ml of 0.5 per cent w/v solution of *2,6-dichloro quinonechlorimide* in *alcohol*; a blue colour is produced in the first tube rapidly fading and becoming red in a few minutes, but no blue colour is produced in the second tube.

(B) To 2 ml of a 0.5 per cent solution add 0.5 ml of *phosphotungstic acid solution*; a white precipitate is produced.

(C) A solution (1 in 20) gives the reactions of chlorides, Appendix 3.1.

Melting range : Between 204° and 208°, with decomposition, Appendix 5.11.

Clarity and colour of solution : A 5.0 per cent w/v solution is clear or very slightly opalescent and colourless.

pH : Between 2.3 and 3.5, determined in a 5.0 per cent w/v solution, Appendix 5.10.

Heavy metals : Not more than 30 parts per million, determined on 0.67 g by Method B, Appendix 3.2.4.

Light absorption : *Extinction* of a 1-cm layer of a 0.001 per cent w/v solution in *0.1N hydrochloric acid* at the maximum at about 290 nm is about 0.430, Appendix 5.15 A.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

Assay : Weigh accurately about 0.4 g and dissolve in 10 ml of *glacial acetic acid* with aid of gentle heat. Cool, add 10 ml of *mercuric acetate solution* and titrate with *0.1N perchloric acid*, using four drops of *crystal-violet solution* as indicator. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02056 g of $C_8H_{12}ClNO_3$.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Storage : Store in well-closed, light-resistant containers.

Pyridoxine Tablets

Pyridoxine Hydrochloride Tablets

Category : B-group Vitamin.

Dose : Pyridoxine Hydrochloride, 5 to 10 mg daily, or in accordance with the need of the patient.

Usual strength : 5 mg.

Standards : Pyridoxine Tablets contain not less than 95.0 per cent and not more than 115.0 per cent of the stated amount of Pyridoxine Hydrochloride $C_8H_{11}NO_3$,HCl.

Identification : To a quantity of powdered tablets equivalent to about 0.1 g of Pyridoxine Hydrochloride, add about 5 ml of *water*, shake the mixture well, filter and add 3 drops of *ferric chloride test-solution* to the filtrate; an orange to deep red colour is produced.

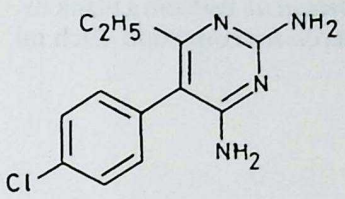
Uniformity of content : Powder one tablet, disperse in about 300 ml of *water* by shaking well and dilute to 500.0 ml with *water*. Filter, discarding the first 25 ml of the filtrate, dilute quantitatively and stepwise with *0.1N hydrochloric acid* to obtain a solution containing about 10 µg of Pyridoxine Hydrochloride per ml. Determine the *extinction* of a 1-cm layer of the resulting solution at the maximum at about 290 nm, Appendix 5.15 A. Calculate the content of $C_8H_{11}NO_3$,HCl in the tablet, using 430 as the value of E(1 per cent, 1-cm) at the maximum at about 290 nm. Repeat the operation with further nine tablets and calculate the average content of the ten tablets. The content of each tablet is between 90 and 110 per cent of the average except that for one tablet the content may be between 85 and 115 per cent of the average.

Other requirements : Comply with the requirements stated under Tablets.

Assay : Weigh and powder 20 tablets. Weigh accurately a quantity of the powder equivalent to about 0.2 g of Pyridoxine Hydrochloride, add 20 ml of *glacial acetic acid* and 5 ml of *mercuric acetate solution*. Warm gently to ensure complete solution of pyridoxine hydrochloride, cool, and titrate with *0.05N perchloric acid*, determining the end-point potentiometrically. Perform a blank determination and make any necessary correction. Each ml of *0.05N perchloric acid* is equivalent to 0.01028 g of $C_8H_{11}NO_3$, HCl.

Storage : Store in well-closed, light-resistant containers.

Pyrimethamine



$C_{12}H_{13}ClN_4$ Mol. Wt. 248.71

Category : Antimalarial.

Dose : Suppressive, 25 mg once a week; therapeutic, 25 to 50 mg once a day for two days.

Description : White, crystalline powder; odourless.

Solubility : Practically insoluble in *water*; slightly soluble in *acetone*, in *alcohol* and in *chloroform*.

Standards : Pyrimethamine is 5-(4-chlorophenyl)-6-ethylpyrimidine-2,4-diamine. It contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of $C_{12}H_{13}ClN_4$, calculated with reference to the dried substance.

Identification : (A) The *infra-red absorption spectrum* exhibits maxima which are only at the same wavelengths as, and have similar relative intensities to, those in the spectrum of *pyrimethamine R.S.*, Appendix 5.15 B.

(B) The light absorption, in the range 230 to 350 nm, of a 1-cm layer of a 0.0015 per cent w/v solution in *0.005N hydrochloric acid*, exhibits a maximum only at 272 nm; *extinction* at 272 nm, about 0.48, Appendix 5.15 A.

(C) To a solution of 50 mg in 5 ml of *2N sulphuric acid*, add 0.2 ml of *potassium mercuri-iodide solution*; a creamy-white precipitate is produced.

(D) Ignite 0.1 g with 0.5g of *anhydrous sodium carbonate*, extract the residue with *water*, and filter. The filtrate, after neutralisation with *nitric acid* gives the reactions of *chlorides*, Appendix 3.1.

Melting range : Between 238° and 242°, Appendix 5.11.

Acidity or Alkalinity : Boil 0.3 g with 15 ml of *water*, cool, and filter. The filtrate is not acid to *methyl red solution* and requires not more than 0.1 ml of *0.05N hydrochloric acid* to make it acid.

Sulphated ash : Not more than 0.1 per cent, Appendix 3.2.7.

Loss on drying : Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°, Appendix 5.8.

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Assay : Weigh accurately about 0.5 g and dissolve in 50 ml of *glacial acetic acid*, warming slightly to effect solution. Cool, add a few drops of *quinaldine red solution* and titrate with *0.1N perchloric acid*. Perform a blank determination and make any necessary correction. Each ml of *0.1N perchloric acid* is equivalent to 0.02487 g of $C_{12}H_{13}ClN_4$.

Storage : Store in tightly-closed, light-resistant containers.

108834

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

Pharmacopoeia of India

(The Indian Pharmacopoeia)

Volume – I
(A – P)

Third Edition
1985

ERRATA

Introduction

Page (xxi)	After	. . Iodoxyl Injection
	Insert	. . Ipecacuanha

Aminocaproic Acid

Page 29	Assay – 7th line	
	For	. . 0.015120
	Read	. . 0.01312

Benzyl Benzoate

Page 67	Refractive index	
	For	. . 1.5668 and 1.5670
	Read	. . 1.567 and 1.569

Ferrous Gluconate

Page 214	Assay – 9th line	
	For	. . Ferrous sulphate solution
	Read	. . Ferroin sulphate solution

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri

GURUKUL KANGRI LIBRARY		
	Signature	Date
Accession		1/4/94
Classification		23.8.95
Cataloguing		10/9/95
Taxation		9.9.95
Filing		20/9/95
E A R.		20/9/95
Any other		
Checked		20.9.95

Recommended By Dr. R. K. [redacted]. S. Dagar

Faculty of Physical - Education.

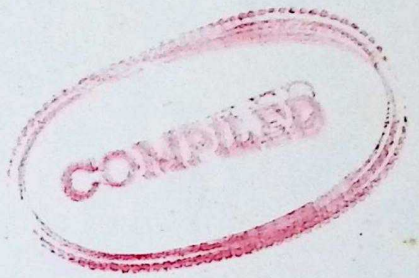
G. K. University

HDR.

STOCK VERIFY 2020 G.K.V. Library

CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri



CC-0. In Public Domain. Gurukul Kangri Collection, Haridwar

Digitized by Arya Samaj Foundation Chennai and eGangotri